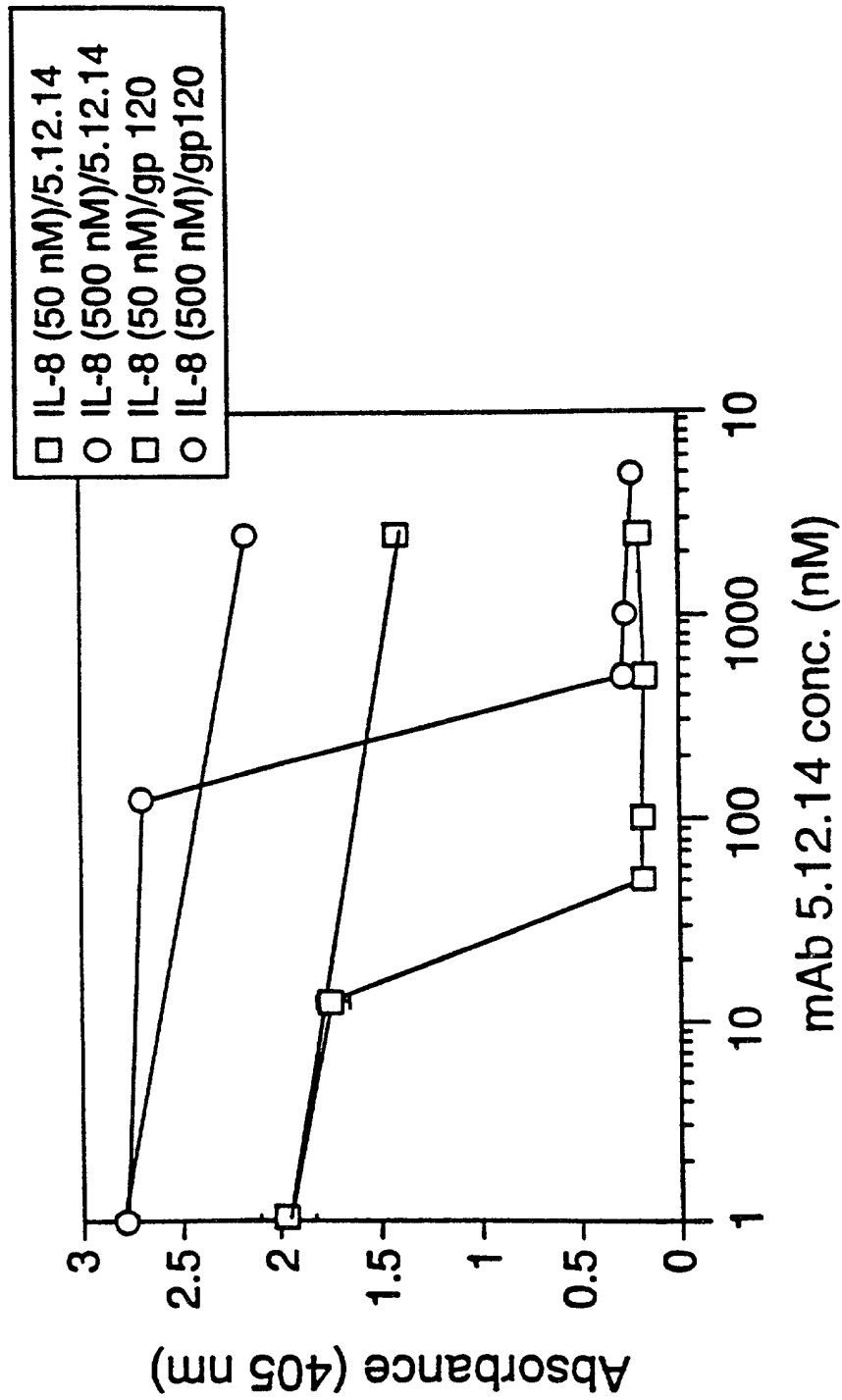


FIG. 1



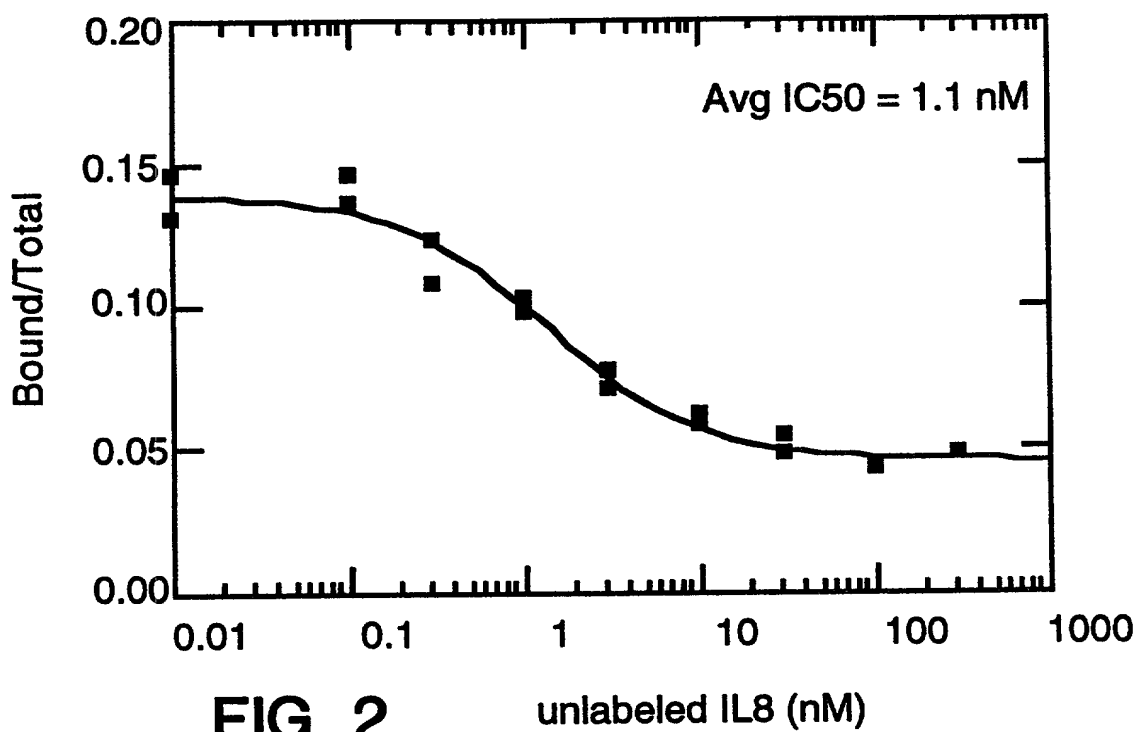


FIG. 2

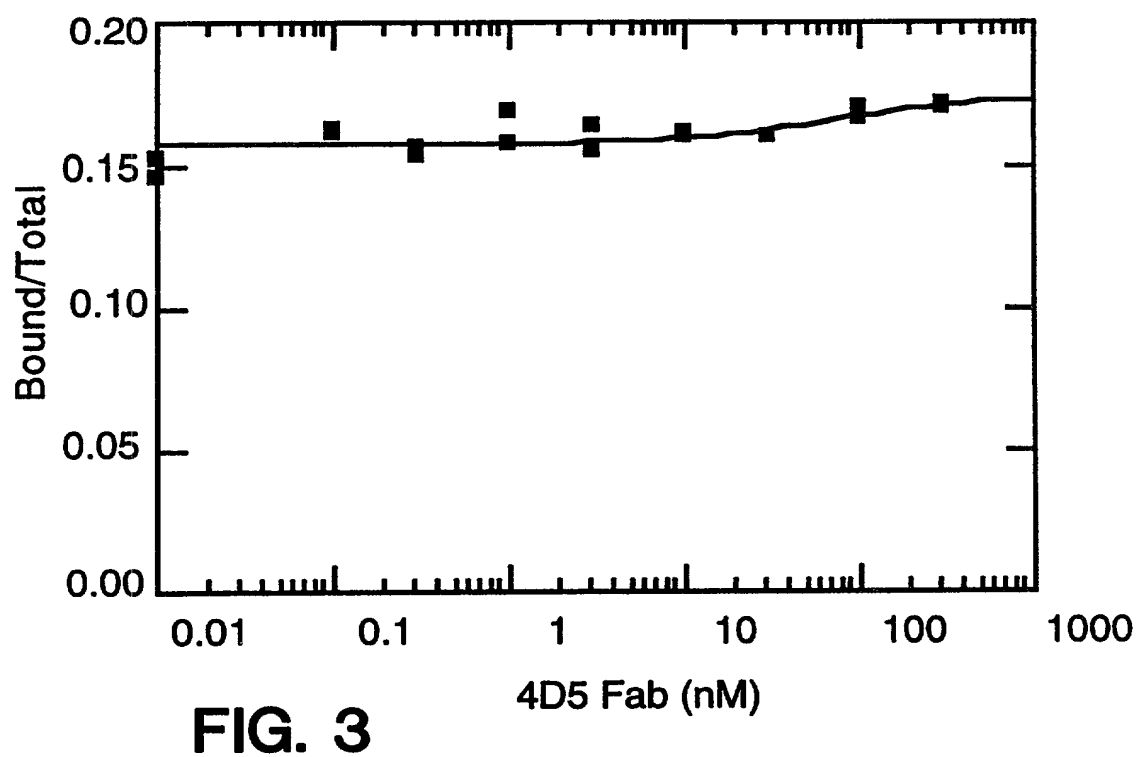
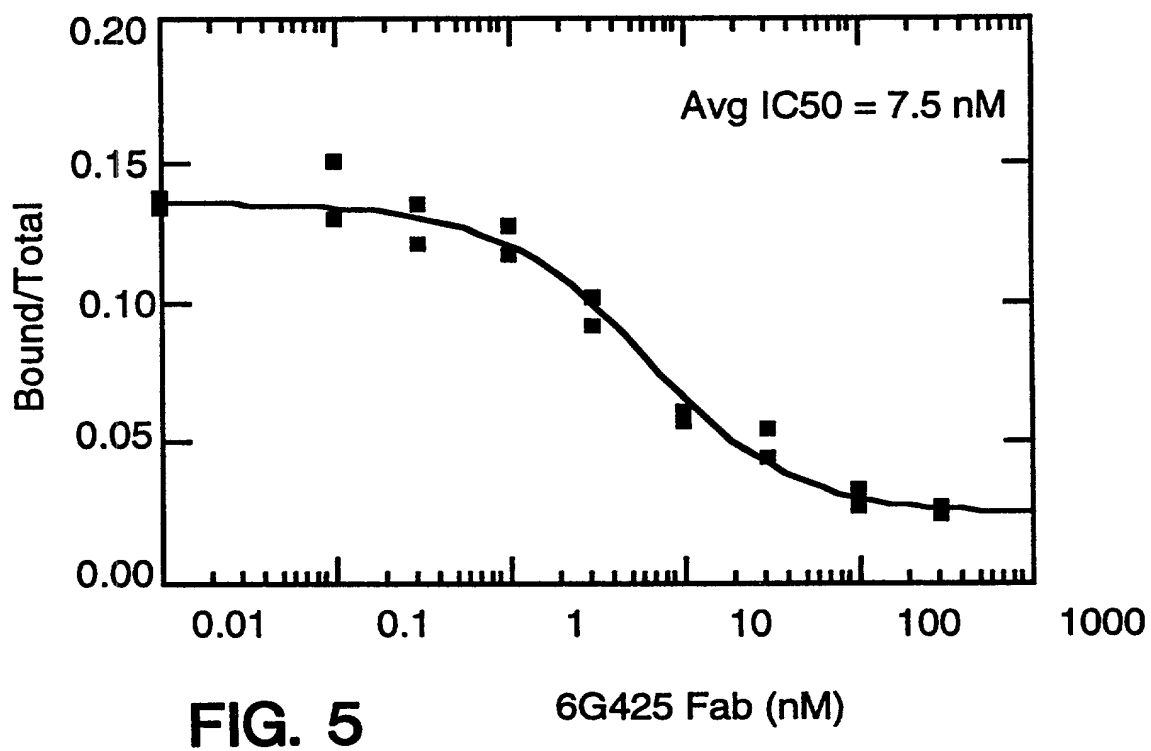
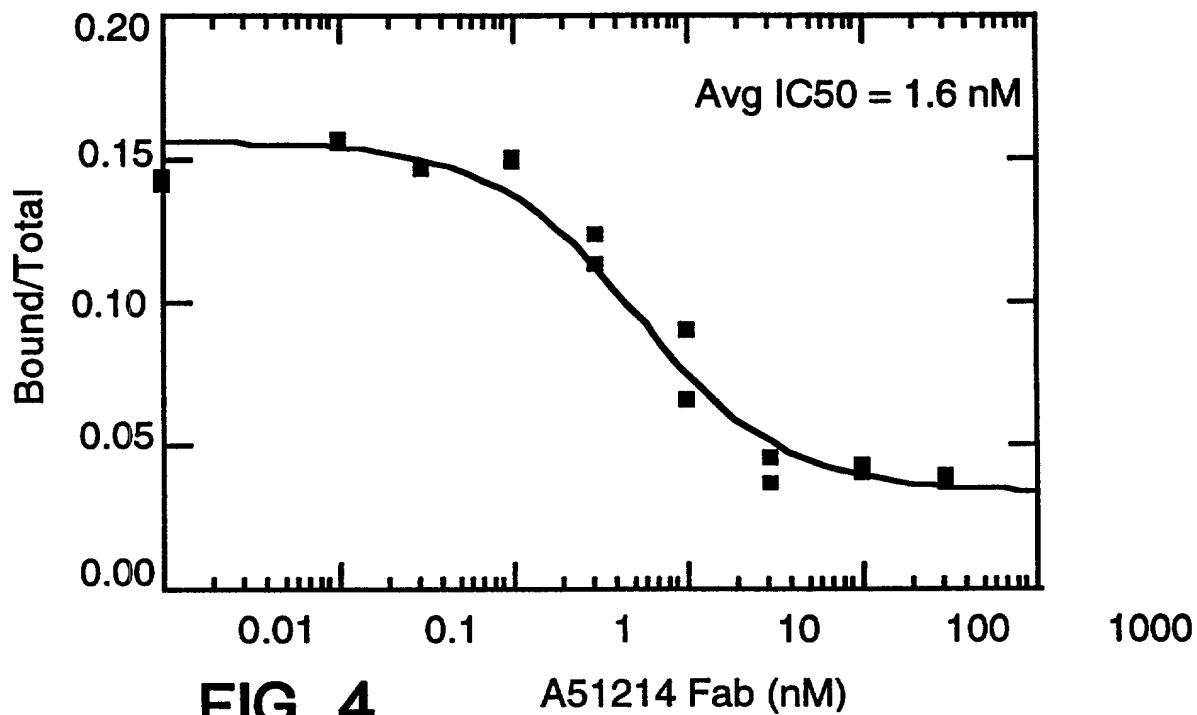


FIG. 3



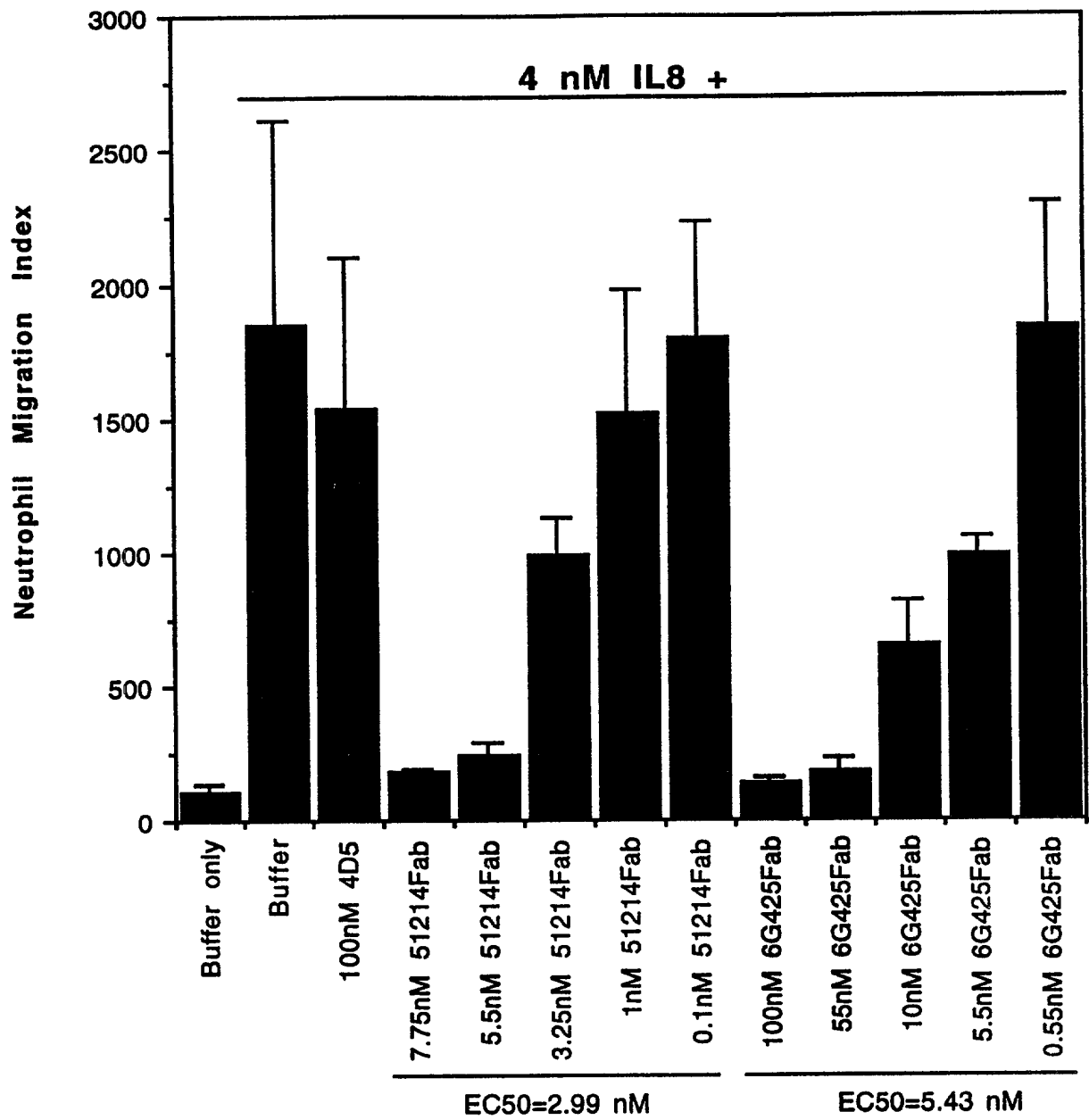


FIG. 6

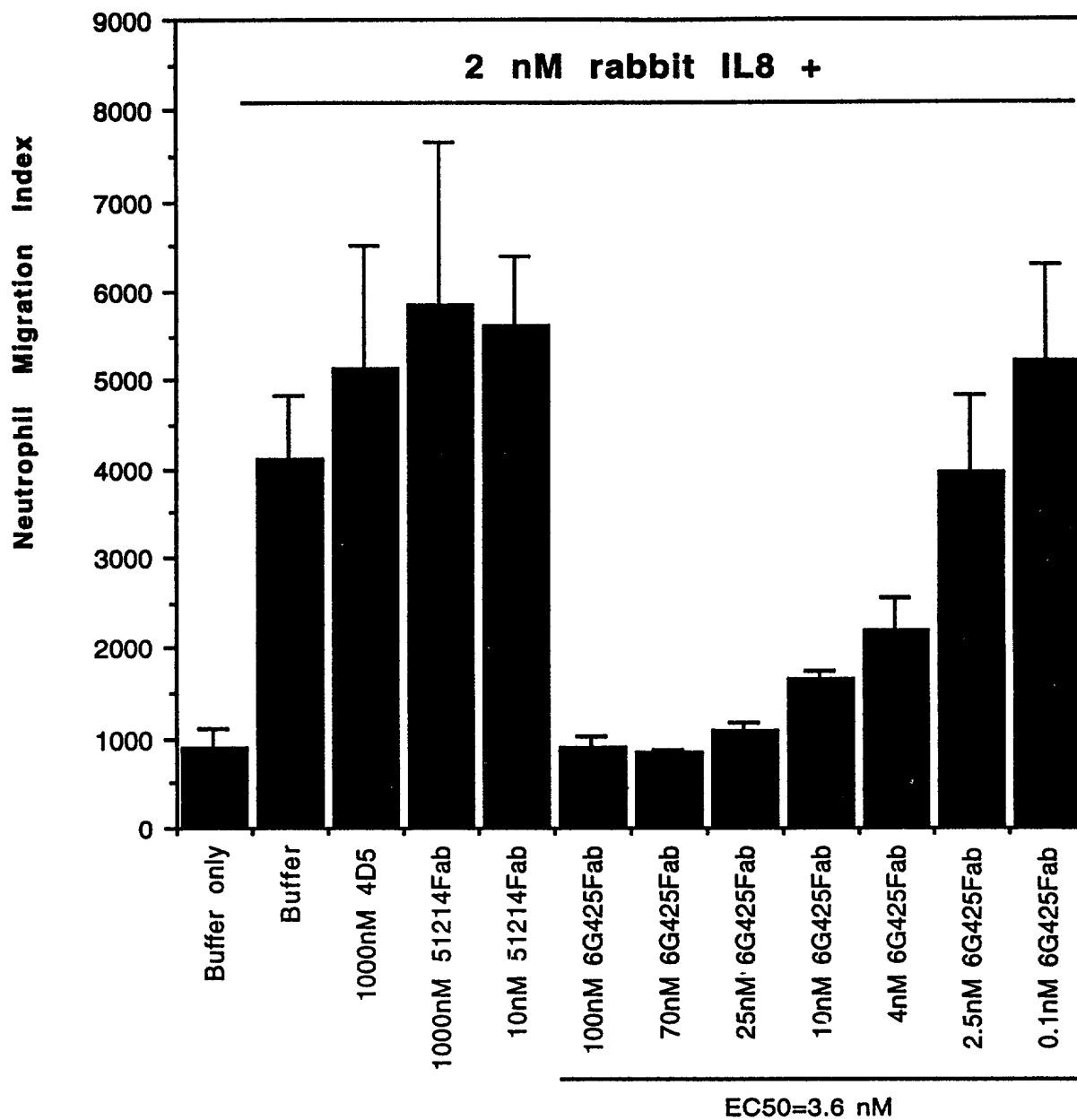


FIG. 7

FIG. 8

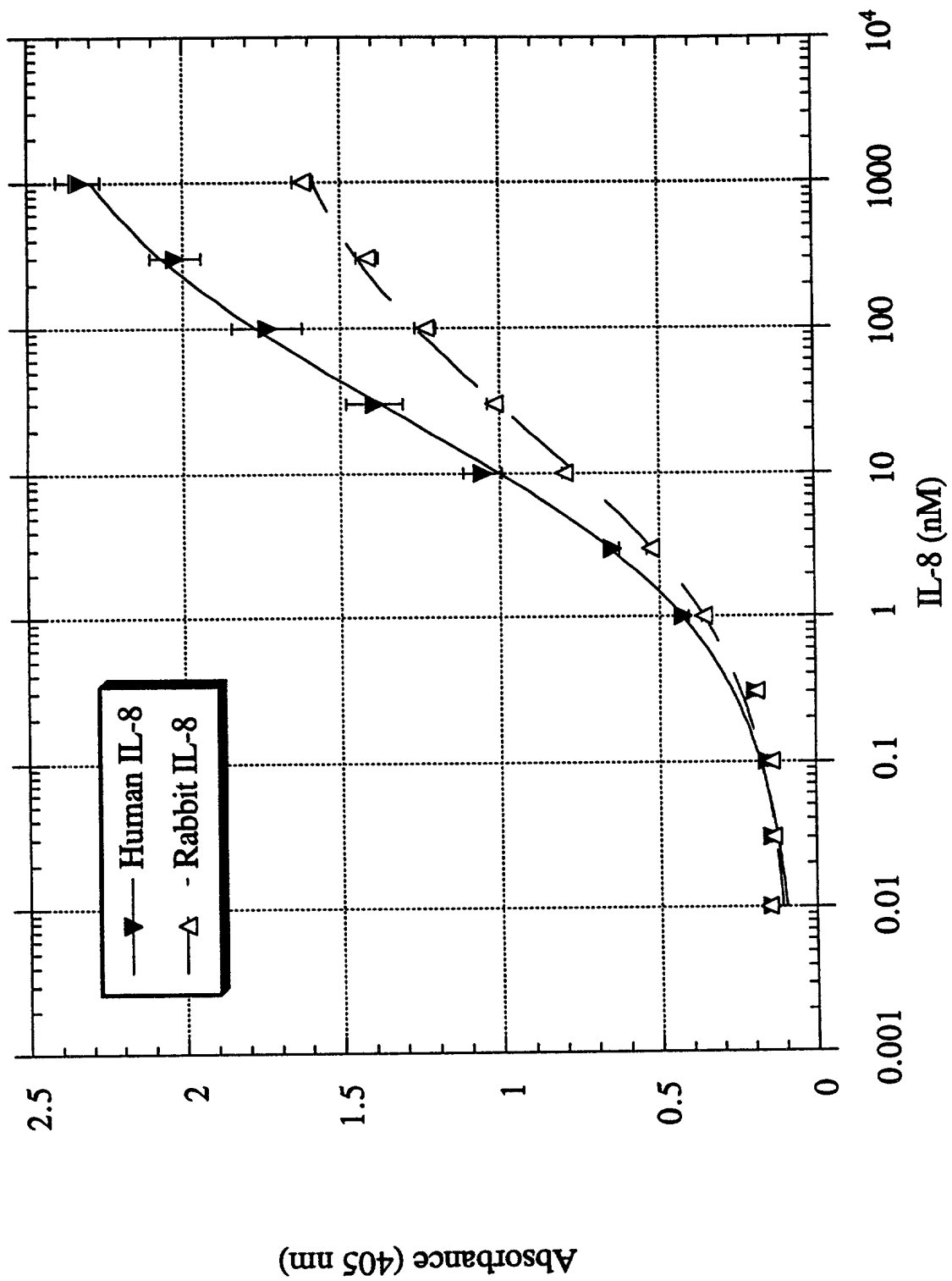
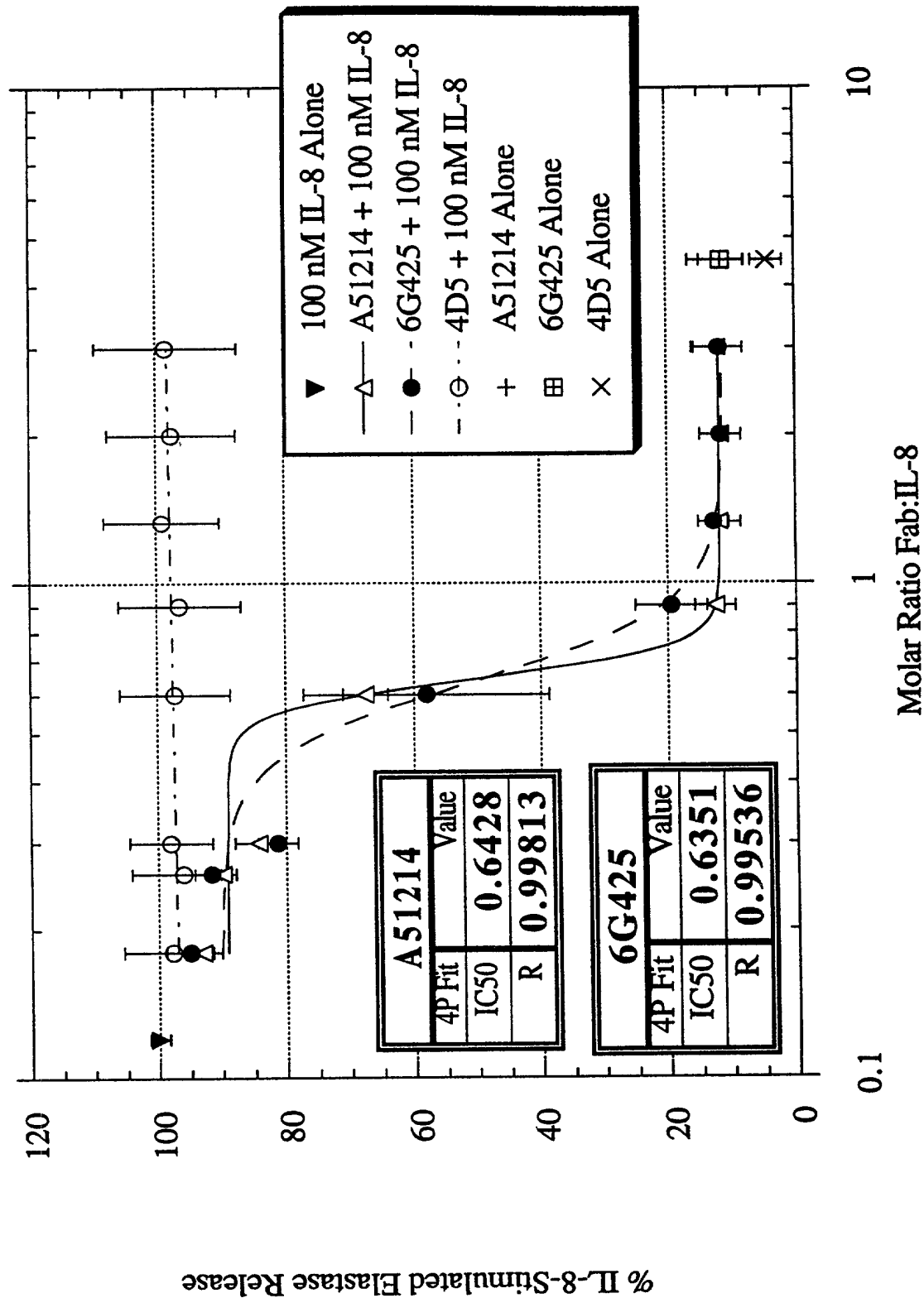
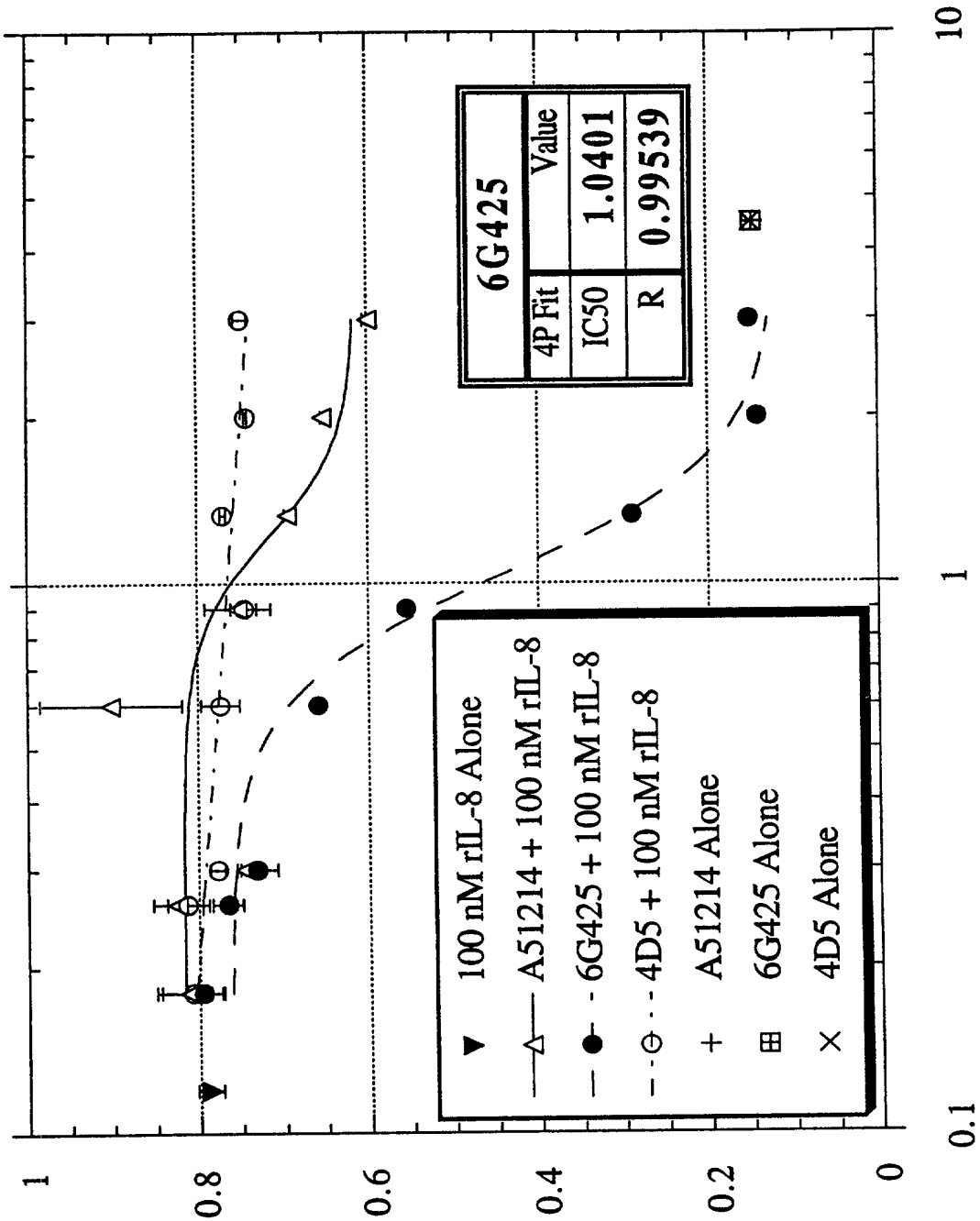


FIG. 9



Absorbance (405 nm)

FIG. 10



Molar Ratio Fab:rIL-8

FIG. 11A and FIG. 11B are bar graphs showing the effect of anti-IL-8 on myeloperoxidase (MPO) and IL-8 levels in tissue. The graphs compare three groups: Untreated (n=6), 17 mg/mL TNBS iv saline (n=14), and 17 mg/mL TNBS iv anti-IL-8 (n=5). The y-axis for FIG. 11A is MPO/minute (mean±SEM) and for FIG. 11B is pg/mg Tissue (mean±SEM).

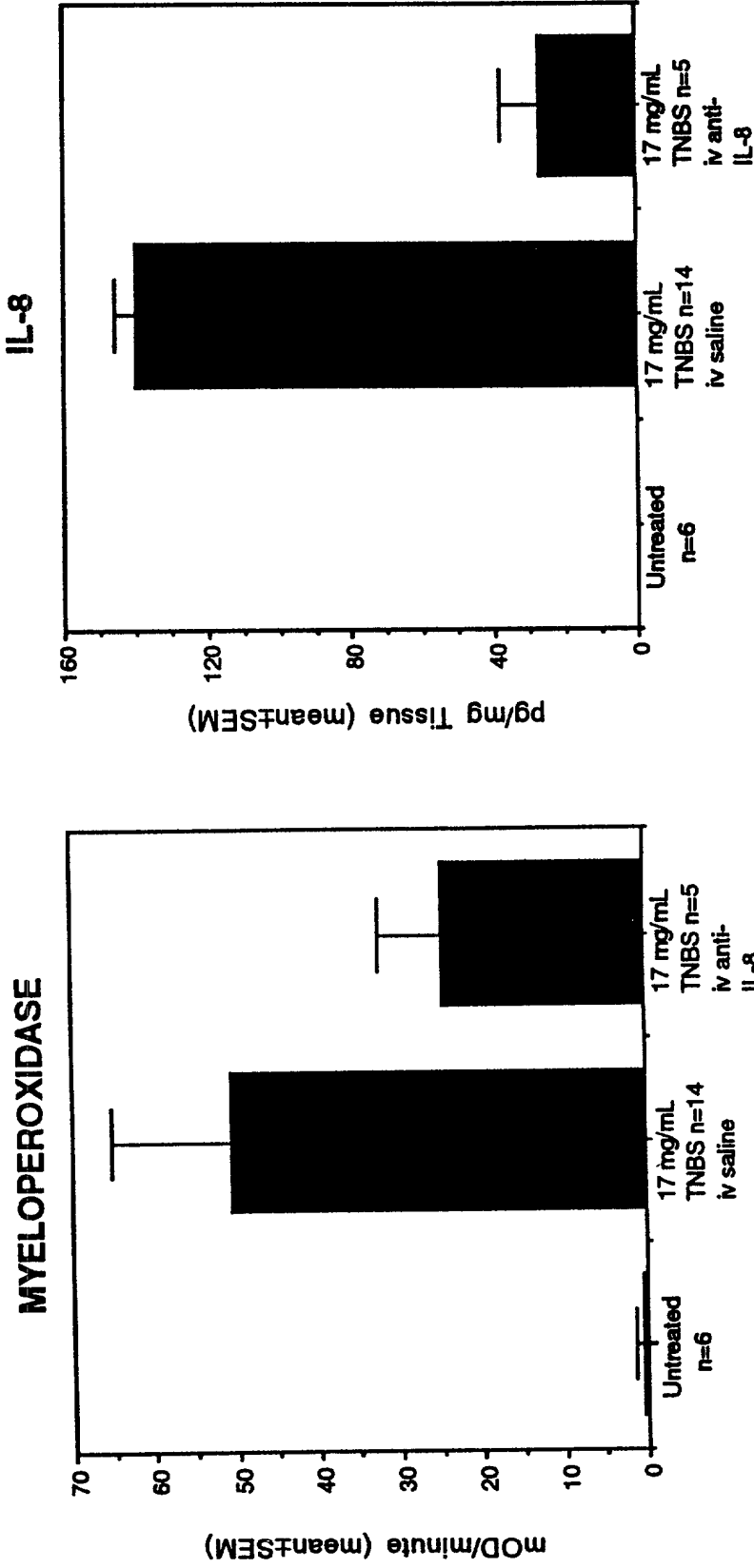


FIG. 11B

FIG. 11A

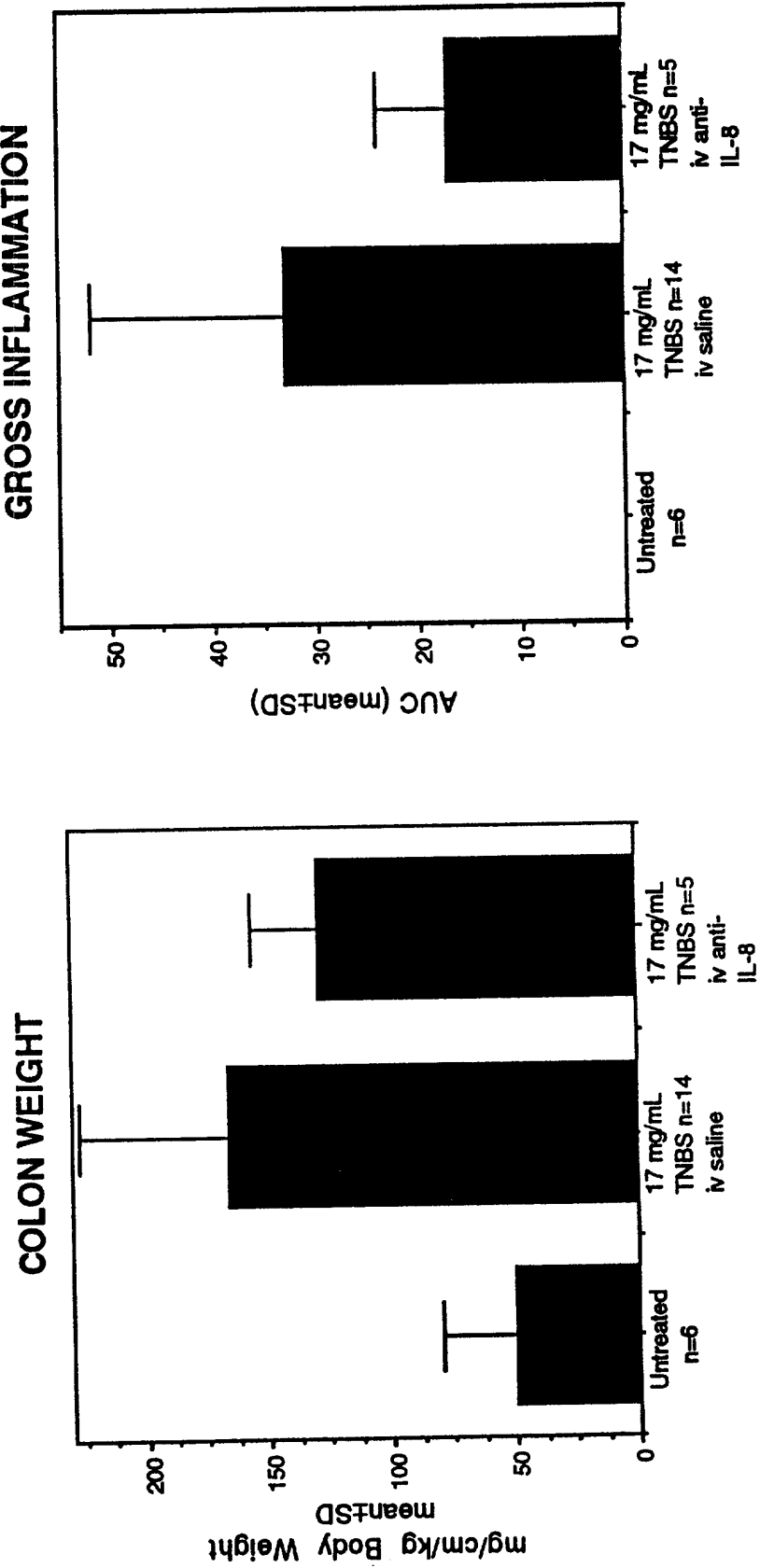


FIG. 11C

FIG. 11D

FIG. 11E

EDEMA

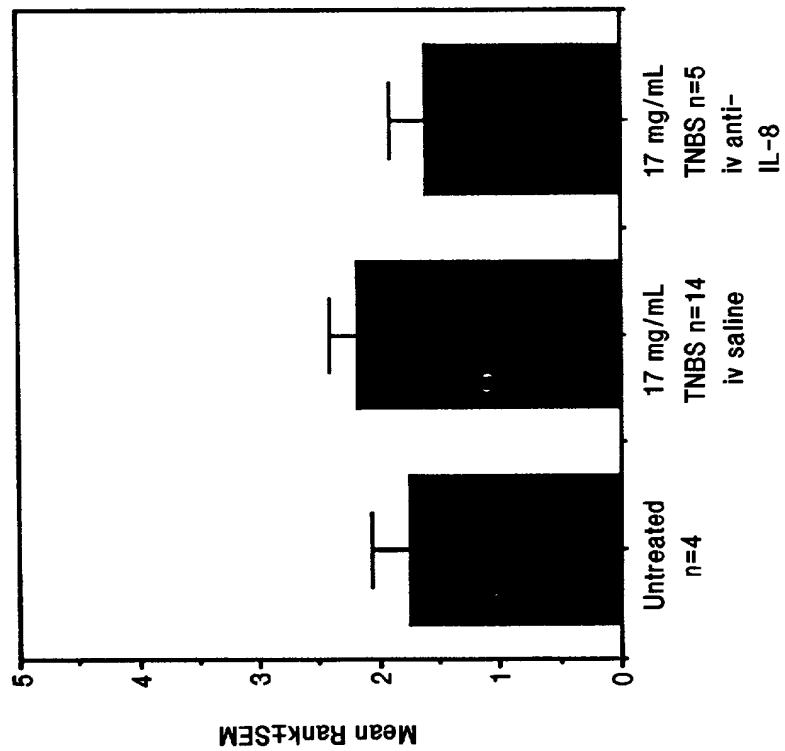


FIG. 11E

EXTENT OF NECROSIS

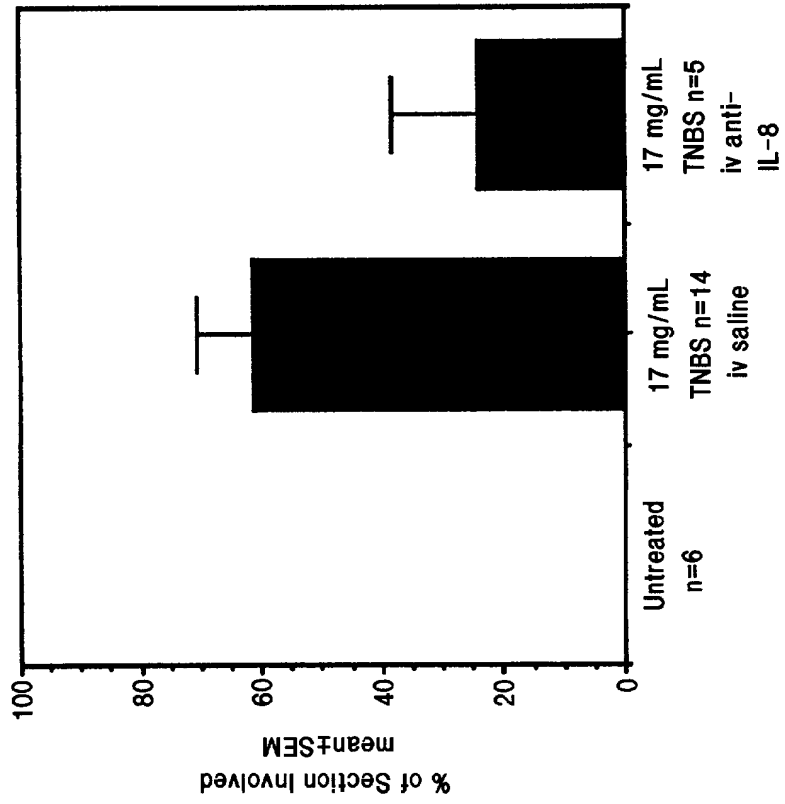


FIG. 11F

that have been shown to be effective in the treatment of various types of cancer, including breast, lung, and colon cancer. The use of these agents in combination with other therapies, such as chemotherapy and radiation, has been shown to improve outcomes in patients with advanced cancer. The goal of this study is to evaluate the efficacy and safety of this combination therapy in patients with advanced cancer.

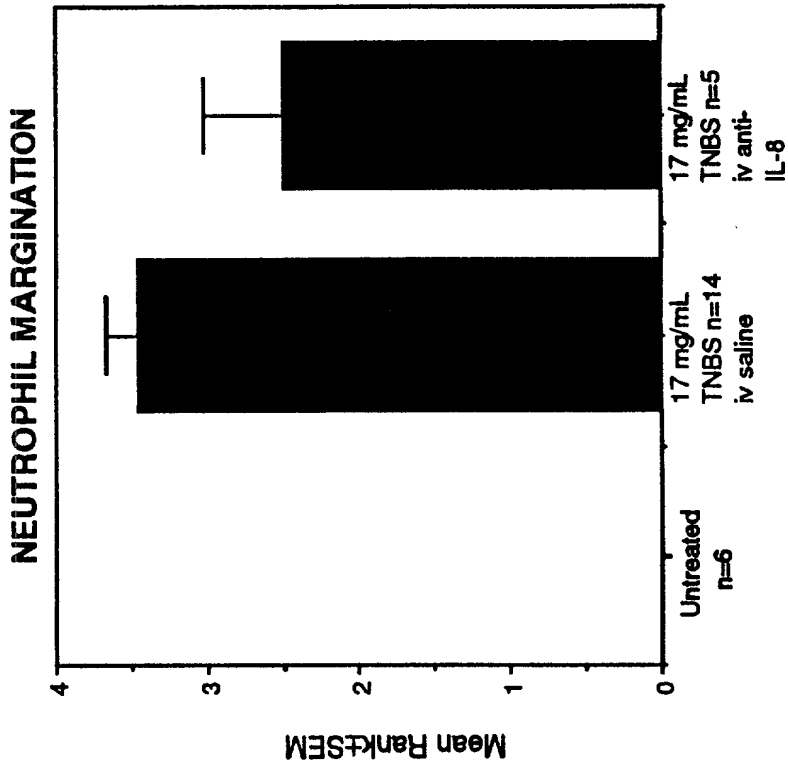


FIG. 11H

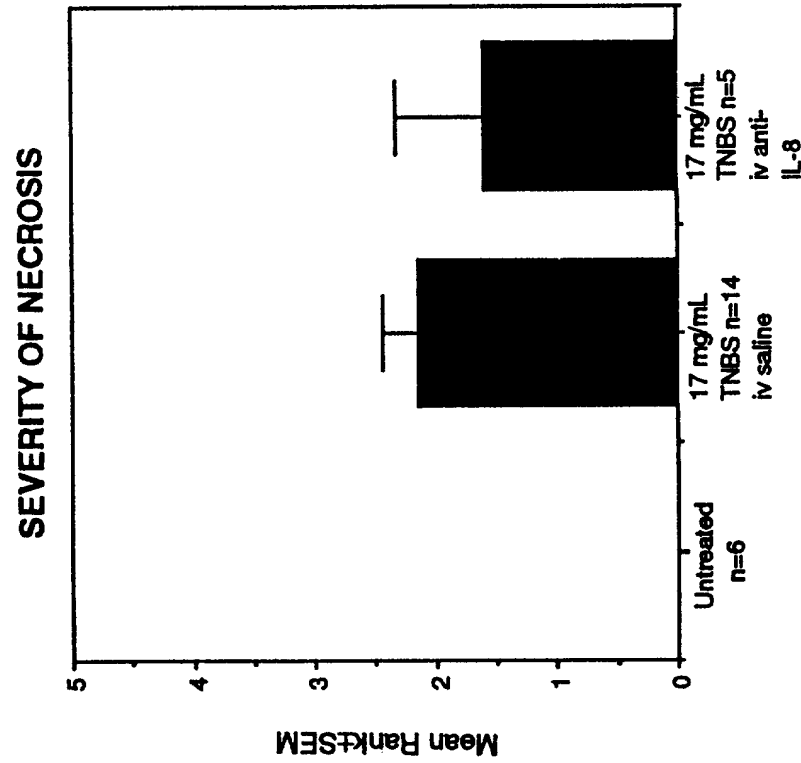


FIG. 11G

FIG. 11I and FIG. 11J are bar graphs showing the mean RanktSEM for neutrophil and mononuclear infiltration, respectively, in the lungs of mice treated with 17 mg/mL TNBS or saline, with or without anti-IL-8 treatment. The y-axis represents the mean RanktSEM, ranging from 0 to 5. The x-axis shows the treatment groups. Error bars represent the standard error of the mean (SEM). Statistical significance is indicated by asterisks (*p < 0.05, **p < 0.01, ***p < 0.001).

NEUTROPHIL INFILTRATION

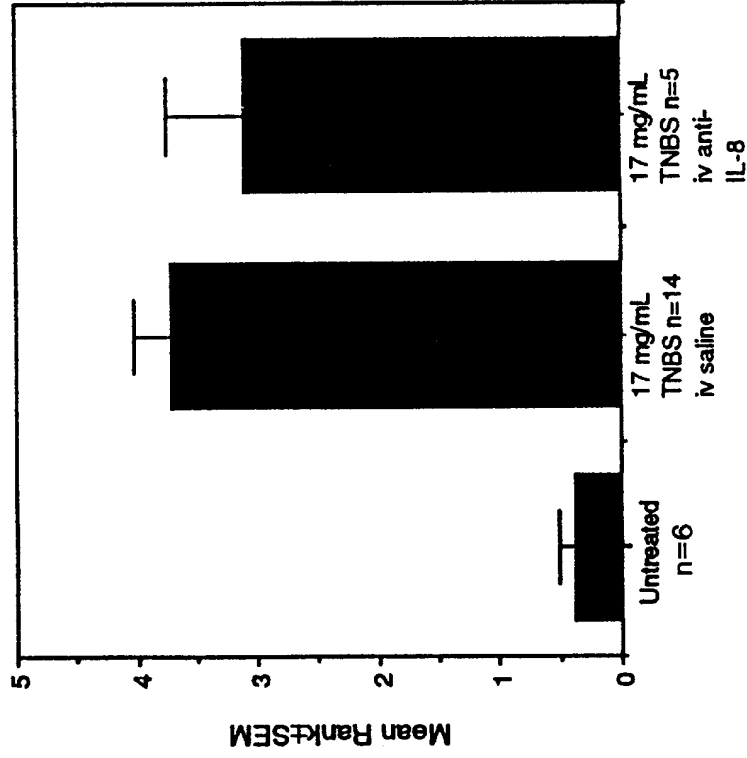


FIG. 11I

MONONUCLEAR INFILTRATION

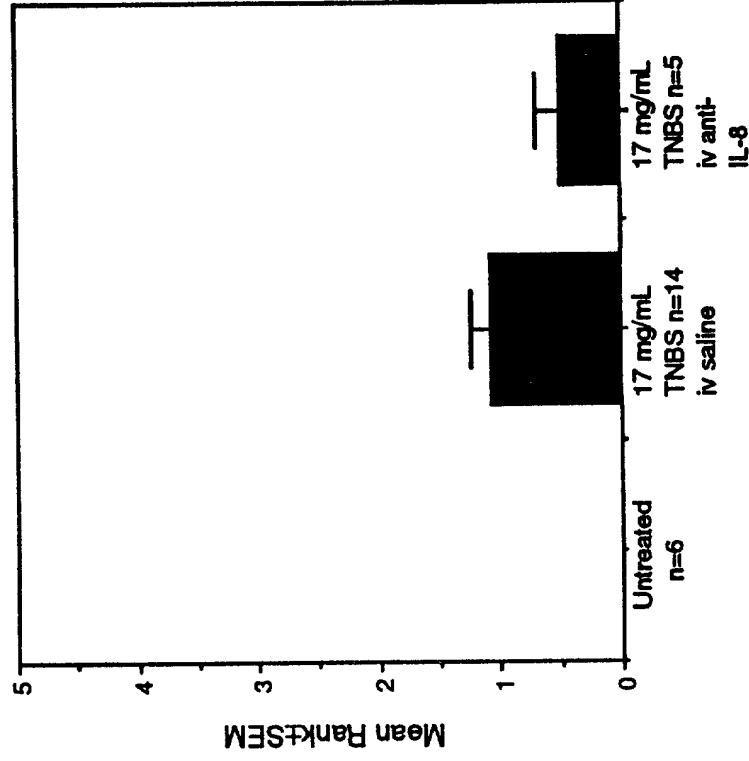
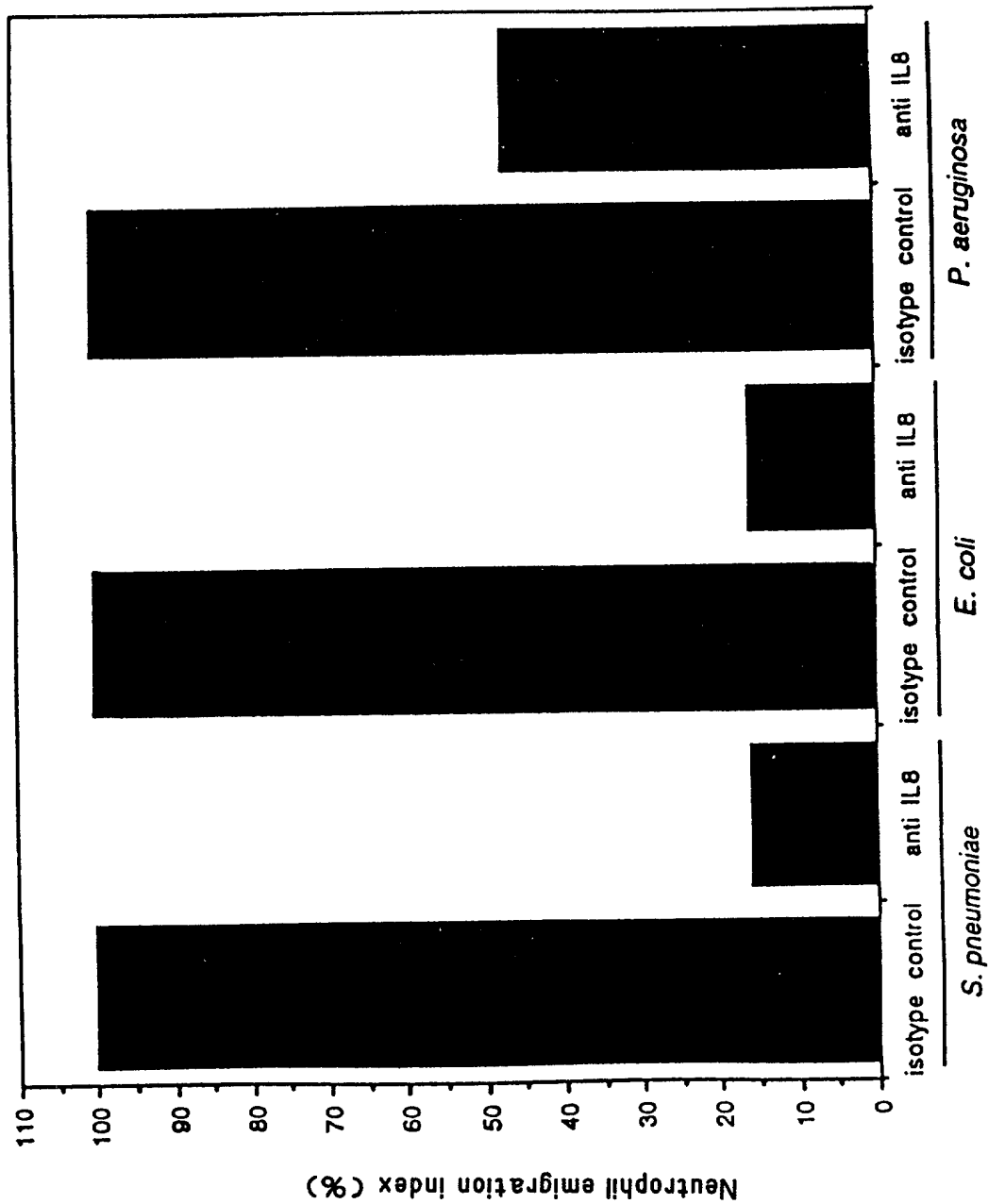


FIG. 11J

FIG. 12



Group (n=5 rabbits per group)

[illegible]

FIG. 13

5' CAGTCCAACGTGTCAGGACGCC 3'

5' GTGCTGCTCATGCTGTAGGTGC 3'

5' GTGCTGCTCATGCTGTAGGTGC 3'

5' GAAGTTGATGTCTTGTGAGTGGC 3'

5' GAAGTTGATGTCTTGTGAGTGGC 3'

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3'

5' CACTGGCTCAGGGAAATAACCC 3'

5' CACTGGCTCAGGGAAATAACCC 3'

5' GGAGAGCTGGGAAGGTGTGCAC 3'

5' GGAGAGCTGGGAAGGTGTGCAC 3'

FIG. 14

Light chain forward primer

SL001A-2 35 mer

5' ACAAACGCGTACGCT GACATCGTCATGACCCAGTC 3'
 T T T
 A

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGGAAGATGGATAACAGTTGGTGC 3'

Heavy chain forward primer

FIG. 15

SL002B 39 mer

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTTGGC 3'

T

C

G

A

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTTGGC 3'

T

A

G

1 GACATTGTCA TGACACAGTC TCAAAAATTC ATGTCCACAT CAGTAGGAGA CAGGGTCAGC
CTGTAACAGT ACTGTGTCAG AGTTTTTAAG TACAGGTGTA GTCATCCTCT GTCCCAGTCG
1 D I V M T Q S Q K F M S T S V G D R V S

61 GTCACCTGCA AGGCCAGTCA GAATGTGGGT ACTAATGTAG CCTGGTATCA ACAGAAACCA
CAGTGGACGT TCCGGTCAGT CTTACACCCA TGATTACATC GGACCATAGT TGTCITTGGT
21 V T C K A S O N V G T N V A W Y Q Q K P
* * * * *

CDR #1

121 GGGCAATCTC CTAAAGCACT GATTACTCG TCATCCTACC GGTACAGTGG AGTCCCTGAT
CCCGTTAGAG GATTTCGTGA CTAAATGAGC AGTAGGATGG CCATGTCACC TCAGGGACTA
41 G Q S P K A L I Y S S Y R Y S G V P D
* * * * *

CDR #2

181 CGCTTCACAG GCAGTGGATC TGGGACAGAT TTCACTCTCA CCATCAGCCA TGTGCAGTCT
GCCAAGTGTC CGTCACCTAG ACCCTGTCTA AAGTGAGAGT GGTAGTCGGT ACACGTCAGA
61 R F T G S G S G T D F T L T I S H V Q S

241 GAAGACTTGG CAGACTATTT CTGTCAGCAA TATAACATCT ATCCTCTCAC GTTCGGTCCT
CTTCTGAACC GTCTGATAAA GACAGTCGTT ATATTGTAGA TAGGAGAGTG CAAGCCAGGA
81 E D L A D Y F C Q Q Y N I Y P L T F G P
* * * * *

CDR #3

301 GGGACCAAGC TGGAGTTGAA ACGGGCTGAT GCTGCACCAC CAACTGTATC CATCTTCCCA
CCCTGGTTCG ACCTCAACTT TGCCCGACTA CGACGTGGTG GTTGACATAG GTAGAAGGGT
101 G T K L E L K R A D A A P P T V S I F P

BstBI

361 CCATTTCGAA

GGTAAGCTT

121 P F E

FIG. 16

```

1  TTCTATTGCT  ACAAACGCGT  ACGCTGAGGT  GCAGCTGGTG  GAGTCTGGGG  GAGGCTTAGT
   AAGATAACGA  TGTTTGCGCA  TGC GACTCCA  CGTCGACCAC  CTCAGACCCC  CTCCGAATCA
1      E  V  Q  L  V  E  S  G  G  G  L  V

61  GCCGCCTGGA  GGGTCCCTGA  AACTCTCCTG  TGCAGCCTCT  GGATTCATAT  TCAGTAGTTA
   CGGCGGACCT  CCCAGGGACT  TTGAGAGGAC  ACGTCGGAGA  CCTAAGTATA  AGTCATCAAT
13  P  P  G  G  S  L  K  L  S  C  A  A  S  G  F  I  F  S  S  Y
                                     *  *

                                CDR #1

121  TGGCATGTCT  TGGGTTTCGCC  AGACTCCAGG  CAAGAGCCTG  GAGTTGGTCG  CAACCATTAA
   ACCGTACAGA  ACCCAAGCGG  TCTGAGGTCC  GTTCTCGGAC  CTCAACCAGC  GTTGGTAATT
33  G  M  S  W  V  R  Q  T  P  G  K  S  L  E  L  V  A  T  I  N
   *  *  *                                     *  *  *

181  TAATAATGGT  GATAGCACCT  ATTATCCAGA  CAGTGTGAAG  GGCCGATTCA  CCATCTCCCG
   ATTATTACCA  CTATCGTGGA  TAATAGGTCT  GTCACACTTC  CCGGCTAAGT  GGTAGAGGGC
53  N  N  G  D  S  T  Y  Y  P  D  S  V  K  G  R  F  T  I  S  R
   *  *  *  *  *  *  *  *  *  *  *  *  *  *  *

                                CDR #2

241  AGACAATGCC  AAGAACACCC  TGTACCTGCA  AATGAGCAGT  CTGAAGTCTG  AGGACACAGC
   TCTGTTACGG  TTCTTTGTGGG  ACATGGACGT  TTA CTGTCA  GACTTCAGAC  TCCTGTGTCG
73  D  N  A  K  N  T  L  Y  L  Q  M  S  S  L  K  S  E  D  T  A

301  CATGTTTTAC  TGTGCAAGAG  CCCTCATTAG  TTCGGCTACT  TGGTTTGGTT  ACTGGGGCCA
   GTACAAAATG  ACACGTTCTC  GGGAGTAATC  AAGCCGATGA  ACCAAACCAA  TGACCCCGGT
93  M  F  Y  C  A  R  A  L  I  S  S  A  T  W  F  G  Y  W  G  Q
                           *  *  *  *  *  *  *  *  *  *

                                CDR #3

361  AGGGACTCTG  GTC ACTGTCT  CTGCAGCCAA  AACAAACAGCC  CCATCTGTCT
   TCCCTGAGAC  CAGTGACAGA  GACGTCGGTT  TTGTTGTCGG  GGTAGACAGA
113  G  T  L  V  T  V  S  A  A  K  T  T  A  P  S  V  Y

```

```

                                ApaI
411  ATCCGGG
      TAGGCCC
130  P

```

FIG. 17

1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG ATATCGTCAT GACACAGTCT CAAAAATTCA TGTCCACATC AGTAGGAGAC
CGCATGCGAC TATAGCAGTA CTGTGTCAGA GTTTTAAAGT ACAGGTGTAG TCATCCTCTG
-3 A Y A D I V M T Q S Q K F M S T S V G D

121 AGGGTCAGCG TCACCTGCAA GGCCAGTCAG AATGTGGGTA CTAATGTAGC CTGGTATCAA
TCCCAGTCGC AGTGGACGTT CCGGTCAGTC TTACACCCAT GATTACATCG GACCATAGTT
18 R V S V T C K A S O N V G T N V A W Y Q
* * * * *

CDR #1

181 CAGAAACCAG GGCAATCTCC TAAAGCACTG ATTTACTCGT CATCCTACCG GTACAGTGGA
GTCTTTGGTC CCGTTAGAGG ATTTTCGTGAC TAAATGAGCA GTAGGATGGC CATGTCACCT
38 Q K P G Q S P K A L I Y S S S Y R Y S G
* * * * *

CDR #2

241 GTCCCTGATC GCTTCACAGG CAGTGGATCT GGGACAGATT TCACTCTCAC CATCAGCCAT
CAGGGACTAG CGAAGTGTCC GTCACCTAGA CCCTGTCTAA AGTGAGAGTG GTAGTCGGTA
58 V P D R F T G S G S G T D F T L T I S H

301 GTGCAGTCTG AAGACTTGGC AGACTATTTT TGTCAGCAAT ATAACATCTA TCCTCTCACG
CACGTCAGAC TTCTGAACCG TCTGATAAAG ACAGTCGTTA TATTGTAGAT AGGAGAGTGC
78 V Q S E D L A D Y F C Q Q Y N I Y P L T
* * * * *

CDR #3

BstBI

361 TTCGGTCCTG GGACCAAGCT GGAGCTTCGA AGAGCTGTGG CTGCACCATC TGTCTTCATC
AAGCCAGGAC CCTGGTTCGA CCTCGAAGCT TCTCGACACC GACGTGGTAG ACAGAAGTAG
98 F G P G T K L E L R R A V A A P S V F I

421 TTCCCGCCAT CTGATGAGCA GTTGAAATCT GGAAGTCTT CTGTTGTGTG CCTGCTGAAT
AAGGGCGGTA GACTACTCGT CAACTTTAGA CCTTGACGAA GACAACACAC GGACGACTTA
118 F P P S D E Q L K S G T A S V V C L L N

481 AACTTCTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG ATAACGCCCT CCAATCGGGT
TTGAAGATAG GGTCTCTCCG GTTTCATGTC ACCTTCCACC TATTGCGGGA GGTTAGCCCA
138 N F Y P R E A K V Q W K V D N A L Q S G

541 AACTCCCAGG AGAGTGTCAC AGAGCAGGAC AGCAAGGACA GCACCTACAG CCTCAGCAGC
TTGAGGGTCC TCTCACAGTG TCTCGTCCTG TCGTTCCTGT CGTGGATGTC GGAGTCGTCG
158 N S Q E S V T E Q D S K D S T Y S L S S

601 ACCCTGACGC TGAGCAAAGC AGACTACGAG AAACACAAAG TCTACGCCTG CGAAGTCACC
TGGGACTGCG ACTCGTTTCG TCTGATGCTC TTTGTGTTTC AGATGCGGAC GCTTCAGTGG
178 T L T L S K A D Y E K H K V Y A C E V T

661 CATCAGGGCC TGAGCTCGCC CGTCACAAAG AGCTTCAACA GGGGAGAGTG
GTAGTCCCGG ACTCGAGCGG GCAGTGTTTC TCGAAGTTGT CCCCTCTCAC
198 H Q G L S S P V T K S F N R G E C

711 TTAA
AATT
216 O

FIG. 19

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCTG TTTTCTCTAT TGCTACAAAC
 TACTTTTCTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
 -23 M K K N I A F L L A S M F V F S I A T N
 61 GCGTACGCTG AGGTGCAGCT GGTGGAGTCT GGGGGAGGCT TAGTGCCGCC TGGAGGGTCC
 CGCATGCGAC TCCACGTCGA CCACCTCAGA CCCCTCCGA ATCACGGCGG ACCTCCCAGG
 -3 A Y A E V Q L V E S G G G L V P P G G S
 121 CTGAAACTCT CCTGTGCAGC CTCTGGATTCT ATATTCAGTA GTTATGGCAT GTCTTGGGTT
 GACTTTGAGA GGACACGTCG GAGACCTAAG TATAAGTCAT CAATACCGTA CAGAACCCAA
 18 L K L S C A A S G F I F S S Y G M S W V
 * * * * *

CDR #1

181 CGCCAGACTC CAGGCAAGAG CCTGGAGTTG GTCGCAACCA TTAATAATAA TGGTGATAGC
 GCGGTCTGAG GTCCGTTCTC GGACCTCAAC CAGCGTTGGT AATTATTATT ACCACTATCG
 38 R Q T P G K S L E L V A T I N N N G D S
 * * * * *

241 ACCTATTATC CAGACAGTGT GAAGGGCCGA TTCACCATCT CCCGAGACAA TGCCAAGAAC
 TGGATAATAG GTCTGTCACA CTTCCCGGCT AAGTGGTAGA GGGCTCTGTT ACGGTTCTTG
 58 T Y Y P D S V K G R F T I S R D N A K N
 * * * * *

CDR #2

301 ACCCTGTACC TGCAAATGAG CAGTCTGAAG TCTGAGGACA CAGCCATGTT TTACTGTGCA
 TGGGACATGG ACGTTTACTC GTCAGACTTC AGACTCCTGT GTCGGTACAA AATGACACGT
 78 T L Y L Q M S S L K S E D T A M F Y C A
 361 AGAGCCCTCA TTAGTTCGGC TACTTGGTTT GGTTACTGGG GCCAAGGGAC TCTGGTCACT
 TCTCGGGAGT AATCAAGCCG ATGAACCAAA CCAATGACCC CGGTTCCCTG AGACCAGTGA
 98 R A L I S S A T W F G Y W G Q G T L V T
 * * * * *

CDR #3

ApaI

421 GTCTCTGCAG CCTCCACCAA GGGCCCATCG GTCTTCCCCC TGGCACCCCTC CTCCAAGAGC
 CAGAGACGTC GGAGGTGGTT CCCGGGTAGC CAGAAGGGGG ACCGTGGGAG GAGGTTCTCG
 118 V S A A S T K G P S V F P L A P S S K S
 481 ACCTCTGGGG GCACAGCGGC CCTGGGCTGC CTGGTCAAGG ACTACTTCCC CGAACCGGTG
 TGGAGACCCC CGTGTGCGCCG GGACCCGACG GACCAGTTCC TGATGAAGGG GCTTGGCCAC
 138 T S G G T A A L G C L V K D Y F P E P V
 541 ACGGTGTCGT GGAACCTCAGG CGCCCTGACC AGCGGCGTGC ACACCTTCCC GGCTGTCCTA
 TGCCACAGCA CCTTGAGTCC GCGGGACTGG TCGCCGCACG TGTGGAAGGG CCGACAGGAT
 158 T V S W N S G A L T S G V H T F P A V L
 601 CAGTCCTCAG GACTCTACTC CCTCAGCAGC GTGGTGACCG TGCCCTCCAG CAGCTTGGGC
 GTCAGGAGTC CTGAGATGAG GGAGTCGTCG CACCACTGGC ACGGGAGGTC GTCGAACCCG
 178 Q S S G L Y S L S S V V T V P S S S L G

FIG. 20A

661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA
TGGGTCTGGA TGTAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT
198 T Q T Y I C N V N H K P S N T K V D K K
721 GTTGAGCCCA AATCTTGTGA CAAAACTCAC ACATGA
CAACTCGGGT TTAGAACACT GTTTTGAGTG TGTACT
218 V E P K S C D K T H T O

FIG. 20B

Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAACCTGTTTCAGGACGCC 3'

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3'

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3'

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3'

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3'

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3'

FIG. 21

Light chain forward primer

6G4.light.Nsi 36-MER

5' CCAATGCATACGCT GAC ATC GTG ATG ACC CAG ACC CC 3'
 T T T T
 A A

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3'

FIG. 22

Heavy chain forward primer

6G4.heavy.Mlu 32-MER

5' CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG 3'
 T C

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTTGGC 3'
 T
 A
 G

FIG. 23

70 G ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT
 C TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
 1 D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCAG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT
 GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
 18 Q A S I S C R S S Q S L V H G I G N T Y
 * * * * * * * * * * * * * * * *
 CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
 AATGTAACCA TGGACGTCTT CGGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG
 38 L H W Y L Q K P G Q S P K L L I Y K V S
 * * * * * * * * * * * * * * * *
 CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTT AGTGGCAGTG GATCAGGGAC AGATTTTACA
 TTGGCTAAAA GACCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
 58 N R F S G V P D R F S G S G S G T D F T
 * * * * *

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
 GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
 78 L R I S R V E A E D L G L Y F C S Q S T
 * * * * *
 CDR #3

361 CATGTTCCGC TCACGTTCCG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGATGCTGCA
 GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCC ACTACGACGT
 98 H V P L T F G A G T K L E L K R A D A A
 * * * * *

MunI

421 CCAACTGTAT CCATCTTCCC ACCATCCAGT GAGCAATTGA
 GGTTGACATA GGTAGAAGGG TGGTAGGTCA CTCGTTAACT
 118 P T V S I F P P S S E Q L K

FIG. 24

70 G AGATTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
 C TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
 1 E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTCAGTA GCCACTACAT GCACTGGGTG
 CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
 18 V K I S C K A S G Y S F S S H Y M H W V
 * * * * *
 CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
 TTCGTCTCGG TACCTTTCTC GGAAC TCACC TAACCGATGT AAC TAGGAAG GTTACC ACTT
 38 K Q S H G K S L E W I G Y I D P S N G E
 * * * * *
 CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
 TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTA ACT GACATCTGTG TAGAAGGTCG
 58 T T Y N Q K F K G K A T L T V D T S S S
 * * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
 TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
 78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
 TCTCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC
 98 R G D Y R Y N G D W F F D V W G A G T T
 * * * * *

CDR #3

BstEII
 ApaI
 421 GTCACCGTCT CCTCCGCCAA AACCGACAGC CCCATCGGTC TATCCGGGCC
 CAGTGGCAGA GGAGGCGGAT TTGGCTGTCG GGGTAGCCAG ATAGGCCCGG
 118 V T V S S A K T D S P I G L S G P

471 CATC
 GTAG
 135 I

FIG. 25

5' CTTGGTGGAGGCGGAGGAGACG 3'

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3'

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3'

SYN.Apa 22 MER

5' CTTGGTGGAGGCGGAGGAGACG 3'

FIG. 26

1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCG TTTTTCCTAT TGCTACAAAT
 TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTA
 -23 M K K N I A F L L A S M F V F S I A T N

 61 GCATACGCTG ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT
 CGTATGCGAC TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
 -3 A Y A D I V M T Q T P L S L P V S L G D

 121 CAGGCCTCCA TCTCTTGCAG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT
 GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
 18 Q A S I S C R S S O S L V H G I G N T Y
 * * * * * * * * * * * * * * *
 CDR #1

 181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
 AATGTAACCA TGGACGTCTT CGGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG
 38 L H W Y L Q K P G Q S P K L L I Y K V S
 * * * * * * * * * * * * * * *
 CDR #2

 241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTCACA
 TTGGCTAAAA GACCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
 58 N R F S G V P D R F S G S G S G T D F T
 * * * * * * * * * * * * * * *

 301 CTCAGGATCA GCAGAGTGGG GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
 GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
 78 L R I S R V E A E D L G L Y F C S Q S T
 * * * * * * * * * * * * * * *
 CDR #3

 361 CATGTTCCGC TCACGTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGTGCTGCA
 GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCC ACAACGACGT
 98 H V P L T F G A G T K L E L K R A V A A
 * * * * * * * * * * * * * * *

 421 CCAACTGTAT TCATCTTCCC ACCATCCAGT GAGCAATTGA AATCTGGAAC TGCCTCTGTT
 GGTGACATA AGTAGAAGGG TGGTAGGTCA CTCGTAACT TTAGACCTTG ACGGAGACAA
 118 P T V F I F P P S S E Q L K S G T A S V

 481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
 CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
 138 V C L L N N F Y P R E A K V Q W K V D N

 541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
 CGGGAGGTGA GCCCATTTAG GGTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCGTGG
 158 A L Q S G N S Q E S V T E Q D S K D S T

 601 TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
 ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
 178 Y S L S S T L T L S K A D Y E K H K V Y

FIG. 27A

661 GCCTGCGAAG TCACCCATCA GGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCGGACTCG AGCGGCAGT GTTCTCTCGAA GTTGTCCCCT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTAA
CTCACAATT
218 E C O

FIG. 27B

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661 TTGGGCACCC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC
AACCCGTGGG TCTGGATGTA GACGTTGCAC TTAGTGTTTCG GGTGTTGTG GTTCCACCTG
198 L G T Q T Y I C N V N H K P S N T K V D
721 AAGAAAGTTG AGCCCAATC TTGTGACAAA ACTCACACAT GA
TTCCTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CT
218 K K V E P K S C D K T H T O

FIG. 28B

Variable Light Chain Domain

	10	20	abcde	30	40
6G425	DIVMTQTPLSLPVSLGDAQASISCRSSQSLVHGIGNTYLHWYLQKPGQSPKLLIY				
	#	#	#	#	#
F(ab)-1	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTYLHWYQQKPGKAPKLLIY				
	#	#	#	#	#
humκI	DIQMTQSPSSLSASVGDRVTITCRASKTI-----SKYLAWYQQKPGKAPKLLIY				
	=====				
	+++++				
	L1				
	50	60	70	80	90
6G425	YKVSNRFGSGVPDRFSDSGSGTDFTLRISRVEAEDLGLYFCSQSTHVPLTFGAGTKLELKR				
	#	#	#	#	#
F(ab)-1	YKVSNRFGSGVPSRFGSGSGTDFTLTISLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR				
	#	#	#	#	#
humκI	YSGSTLESQVPSRFGSGSGTDFTLTISLQPEDFATYYCQQHNEYPLTFGQGTKVEIKR				
	===				=====
	+++++				+++++
	L2				L3

Variable Heavy Chain Domain

	10	20	30	40
6G425	EIQLQQSGPELMKPGASVKISCKASGYFSSHYMHVVKQSHGKSLEWI			
	#	#	#	#
F(ab)-1	EVQLVESGGGLVQPGGSLRLSCAASGYFSSHYMHVVRQAPGKGLEWV			
	#	#	#	#
humIII	EVQLVESGGGLVQPGGSLRLSCAASGFSFTGHWMNVVRQAPGKGLEWV			
	=====			
	+++++			
	H1			
	50	a	70	80
6G425	GYIDPSNGETTYNQKFKGKATLTVDTSSTANVHLSSLTSDSAVYFCAARGDYRYNGDWFFDVWGAGT			
	#	#	#	#
F(ab)-1	GYIDPSNGETTYNQKFKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAARGDYRYNGDWFFDVWGQGT			
	#	#	#	#
humIII	GMIHPDSETRYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAARGIYFY-GTTYFDYWQGT			
	=====			=====
	+++++			+++++
	H2			H3

FIG. 29

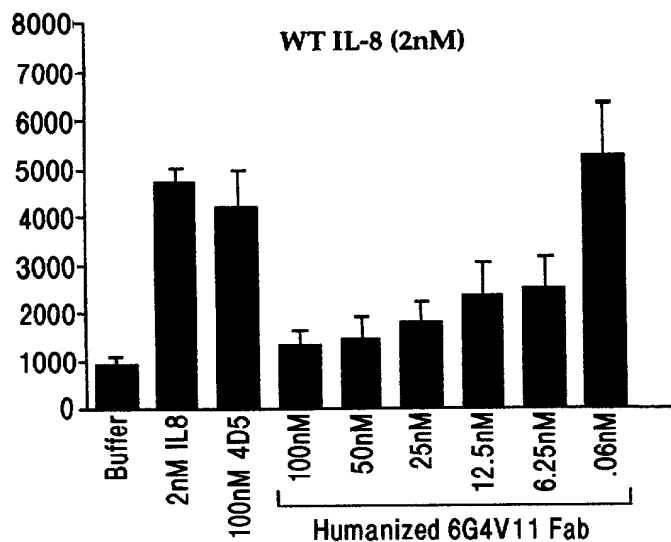


FIG. 30A

IC₅₀~12nM

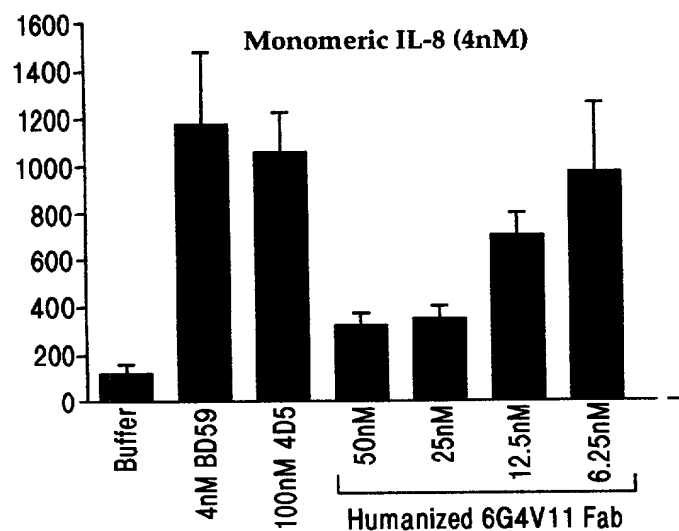


FIG. 30B

IC₅₀~15nM

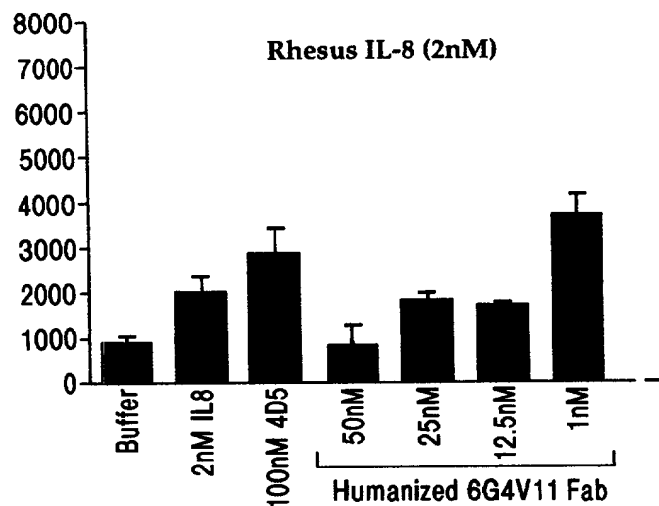


FIG. 30C

IC₅₀~22nM

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTY
LHWYQQKPKAPKLLIYKVSNRFSGVPSRFSGSGGTDFTLTISSLQPEDFATYYCSQST
HVPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLEWVG YIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHHKPSNTK
VDKKVEPKSCDKTHT

Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGGSGGDFDYEKMANANKGAMTENADENALQSDAKGKLDVATDYGAADIGDVS
GLANGATGDFAGSSNSQMAQVGDGDN SPLMNNFRQYLP SLPQSV ECRPFVFSAGKPY
EFSIDCDKINLFRGVFAFLLYVATFMVVFSTFANILRNKES

FIG. 31A

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
 TACTTTTCTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
 -23 M K K N I A F L L A S M F V F S I A T N

 61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
 CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
 -3 A Y A D I Q M T Q S P S S L S A S V G D

 121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TAACACGTAT
 TCCCACTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
 18 R V T I T C R S S Q S L V H G I G N T Y

 181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
 AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
 38 L H W Y Q Q K P G K A P K L L I Y K V S

 241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
 TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
 58 N R F S G V P S R F S G S G S G T D F T

 301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
 GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
 78 L T I S S L Q P E D F A T Y Y C S Q S T

 361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
 GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
 98 H V P L T F G Q G T K V E I K R T V A A

 421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
 GGTAAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
 118 P S V F I F P P S D E Q L K S G T A S V

 481 GTGTGCCTGC TGAATAACTT CTATCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
 CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
 138 V C L L N N F Y P R E A K V Q W K V D N

 541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
 CGGGAGGTTA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCTGTT
 158 A L Q S G N S Q E S V T E Q D S K D S T

 601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
 ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
 178 Y S L S S T L T L S K A D Y E K H K V Y

 661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
 CGGACGCTTC AGTGGGTAGT CCCGACTCG AGCGGGCAGT GTTCTCTGAA GTTGTCCCTT
 198 A C E V T H Q G L S S P V T K S F N R G

 721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
 CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGACCGG GATCATGCGT TGATCAGCAT
 218 E C O

FIG. 31B

FIG. 31C

FIG. 32



FIG. 32

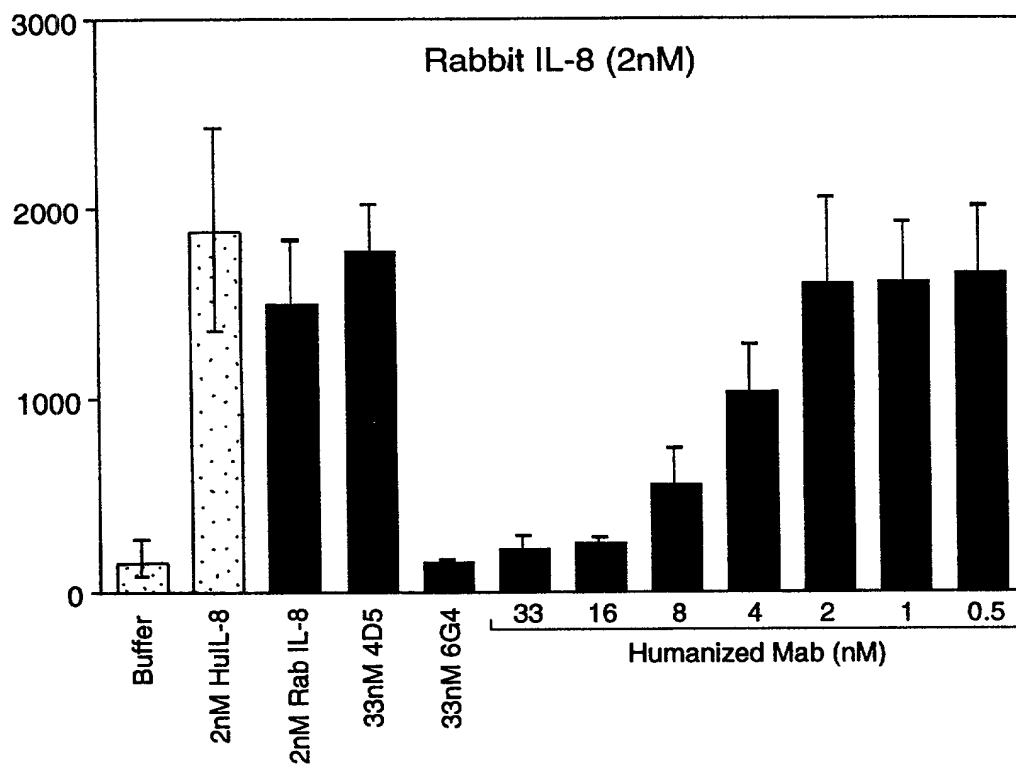
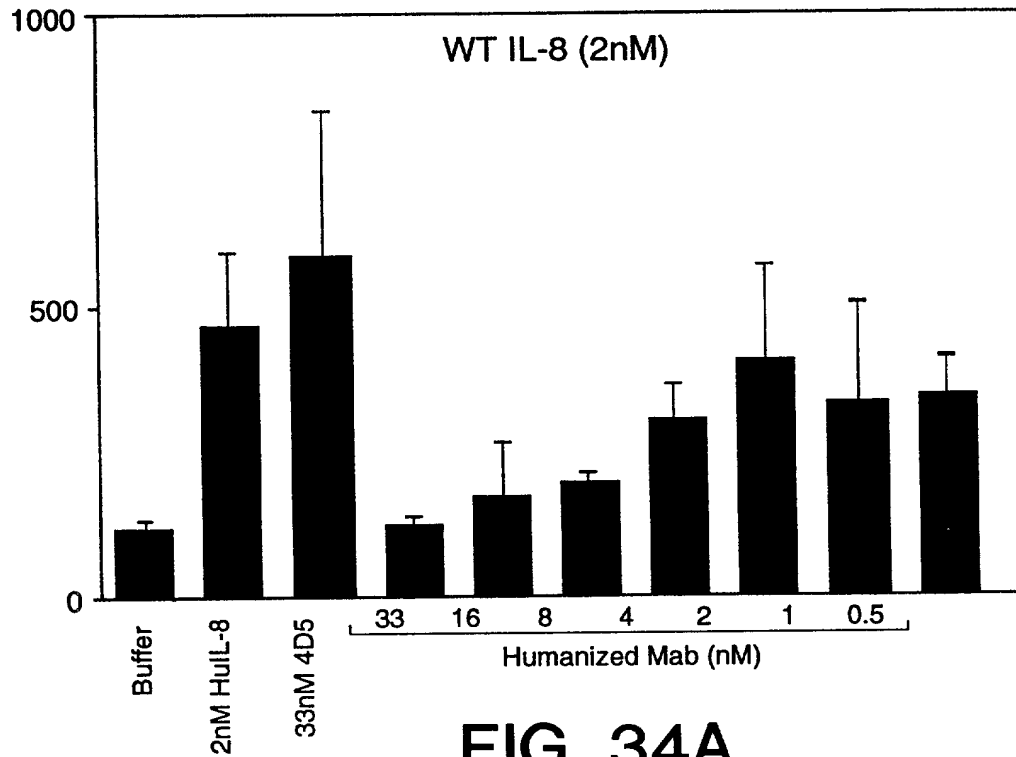


FIG. 34C

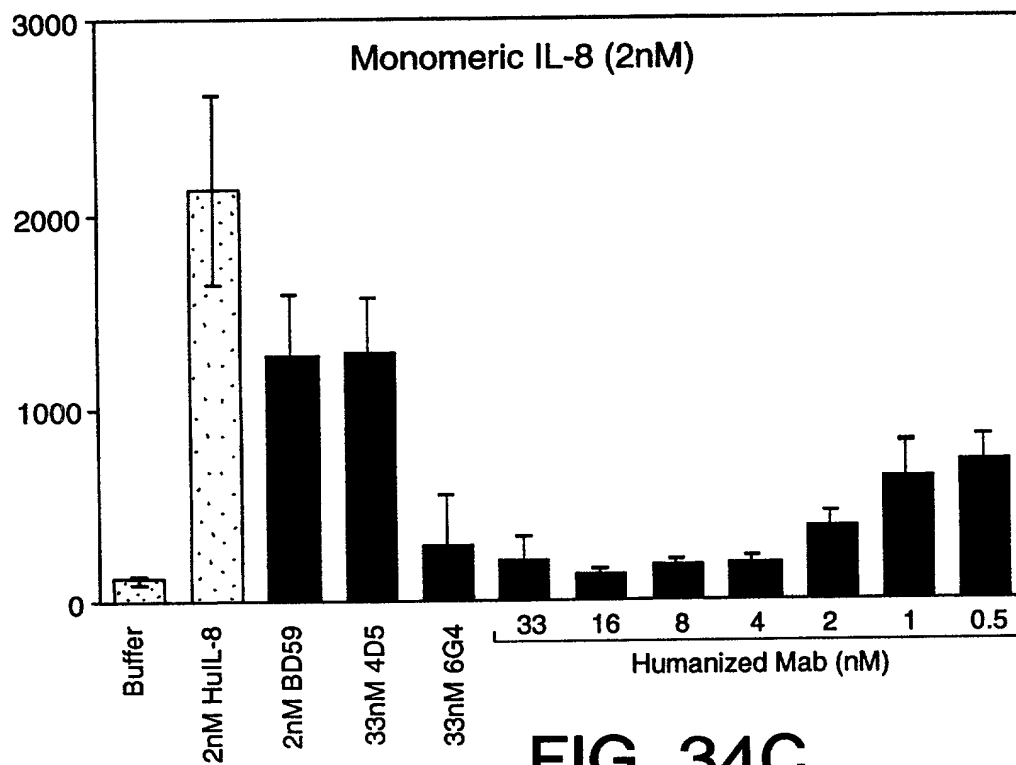


FIG. 34C

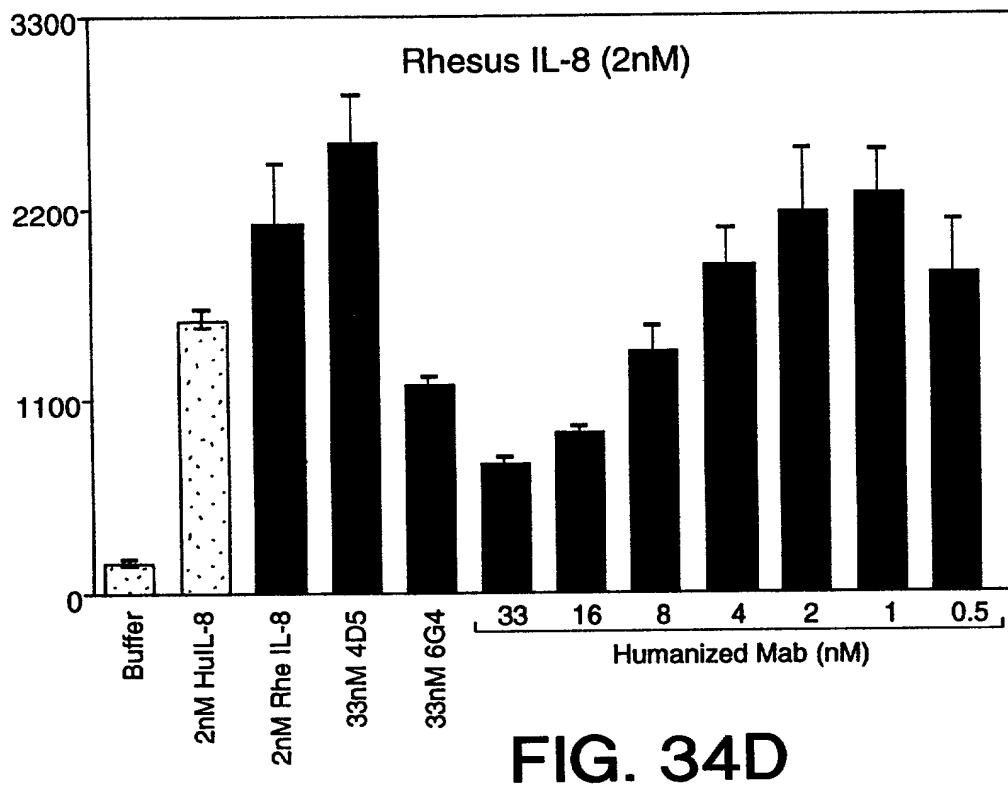


FIG. 34D

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain

MKKNIAFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDVRTITCRSSQSLVHGIGATY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGSGTDTLTISLQPEDFATYYCSQST
HVPLTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSITYLSSTLTLSKADYEKHKVYACEVTHQGLSPVTTKSFNRG
EC

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain

MKKNIAFLLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFEDVWGQGLVTVSSASTKGPSVFLAPSSKSTSGGTAALGCLVKDYF
PEPVTISWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT

Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPELLGGRMKOLEDKVEELL SKNYHLENEVARLKKLVGER

FIG. 35

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
 TACTTTTCTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACATGTTTG
 -23 M K K N I A F L L A S M F V F S I A T N

 61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
 CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
 -3 A Y A D I Q M T Q S P S S L S A S V G D

 121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT
 TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACATGCATA
 18 R V T I T C R S S O S L V H G I G A T Y

 181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
 AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
 38 L H W Y Q Q K P G K A P K L L I Y K V S

 241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
 TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
 58 N R F S G V P S R F S G S G S G T D F T

 301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
 GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
 78 L T I S S L Q P E D F A T Y Y C S Q S T

 361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
 GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
 98 H V P L T F G Q G T K V E I K R T V A A

 421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
 GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
 118 P S V F I F P P S D E Q L K S G T A S V

 481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGA GGTGGATAAC
 CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
 138 V C L L N N F Y P R E A K V Q W K V D N

 541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
 CGGGAGGTTA GCCCATGAG GGTCTCTCTA CAGTGTCTCG TCCTGTCTGT CCTGTCTGTG
 158 A L Q S G N S Q E S V T E Q D S K D S T

 601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
 ATGTGCGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
 178 Y S L S S T L T L S K A D Y E K H K V Y

 661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
 CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTTCCTCGAA GTTGTCCCTT
 198 A C E V T H Q G L S S P V T K S F N R G

 721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
 CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
 218 E C O

FIG. 36

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
 TTTTCCCATA GATCTCCAAC TCCACTAAAA TACTTTTTTCT TATAGCGTAA AGAAGAACGT
 -1 M K K N I A F L L A

841 TCTATGTTTCG TTTTTCCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT
 AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
 -11 S M F V F S I A T N A Y A E V Q L V Q S

901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
 CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
 8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
 AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTTCC GGACCTTACC
 28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
 CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
 48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
 AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
 68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
 CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCTAA TAGCGATGTT ACCACTGACC
 88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
 AAGAAGCTGC AGACCCCAGT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCCG
 108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
 GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC
 128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
 CCGACGGACC AGTTCTTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
 148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
 GACTGGTCGC CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG
 168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
 TCGTCGCACC ACTGGCACGG GAGGTCGTCG AACCCGTGGG TCTGGATGTA GACGTTGCAC
 188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
 TTAGTGTTTCG GGTCGTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
 208 N H K P S N T K V D K K V E P K S C D K

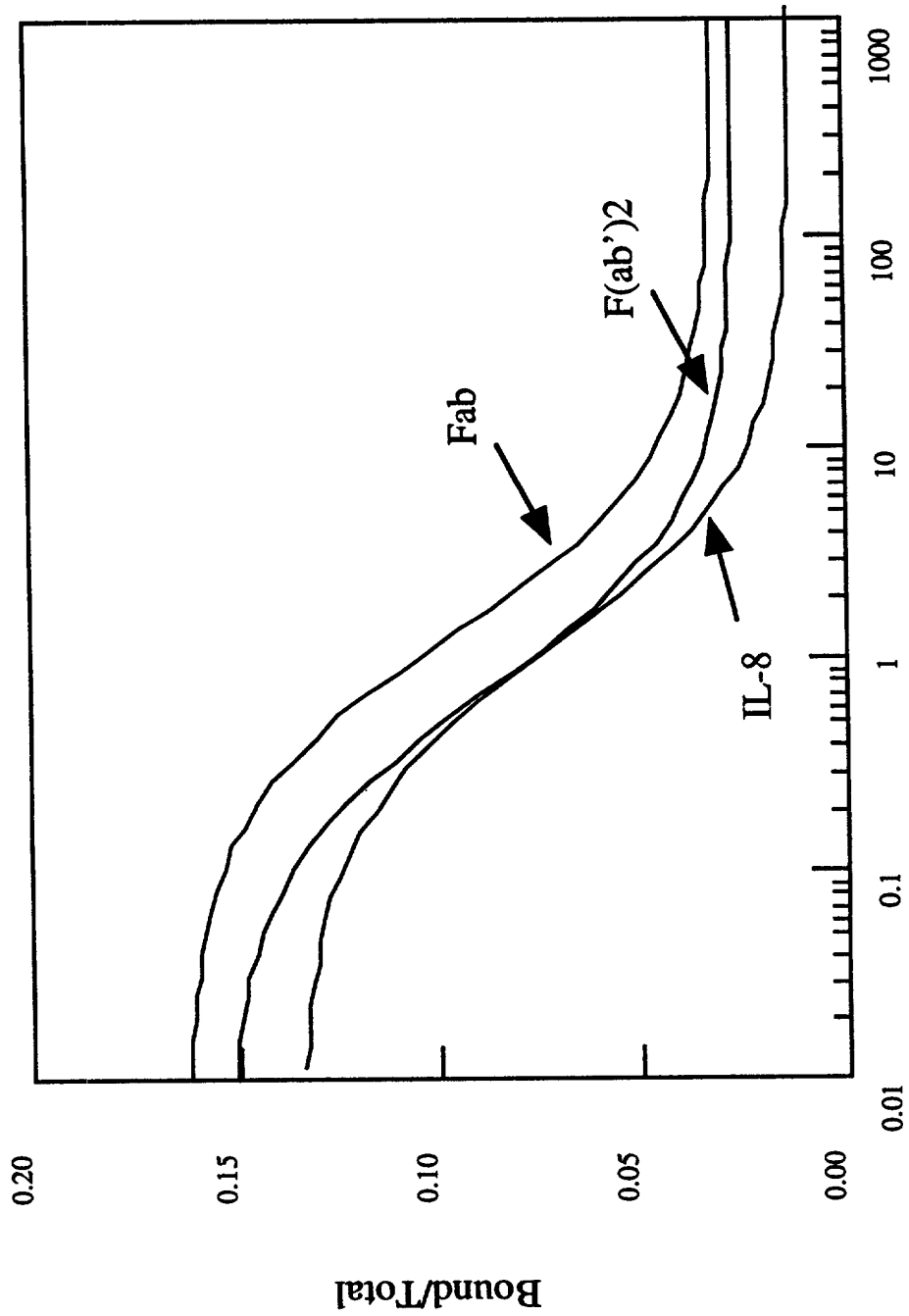
1561 ACTCACACAT GCCCGCCGTG CCCAGCACCA GAACTGCTGG GCGGCCGCAT GAAACAGCTA
 TGAGTGTTGTA CGGGCGGCAC GGGTCGTGGT CTTGACGACC CGCCGGCGTA CTTTGTCTGAT
 228 T H T C P P C P A P E L L G G R M K Q L

FIG. 37A

1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA
CTCCTGTTCC AGCTTCTCGA TGAGAGGTTT TTGATGGTGG ATCTCTTACT TCACCGTTCT
248 E D K V E E L L S K N Y H L E N E V A R

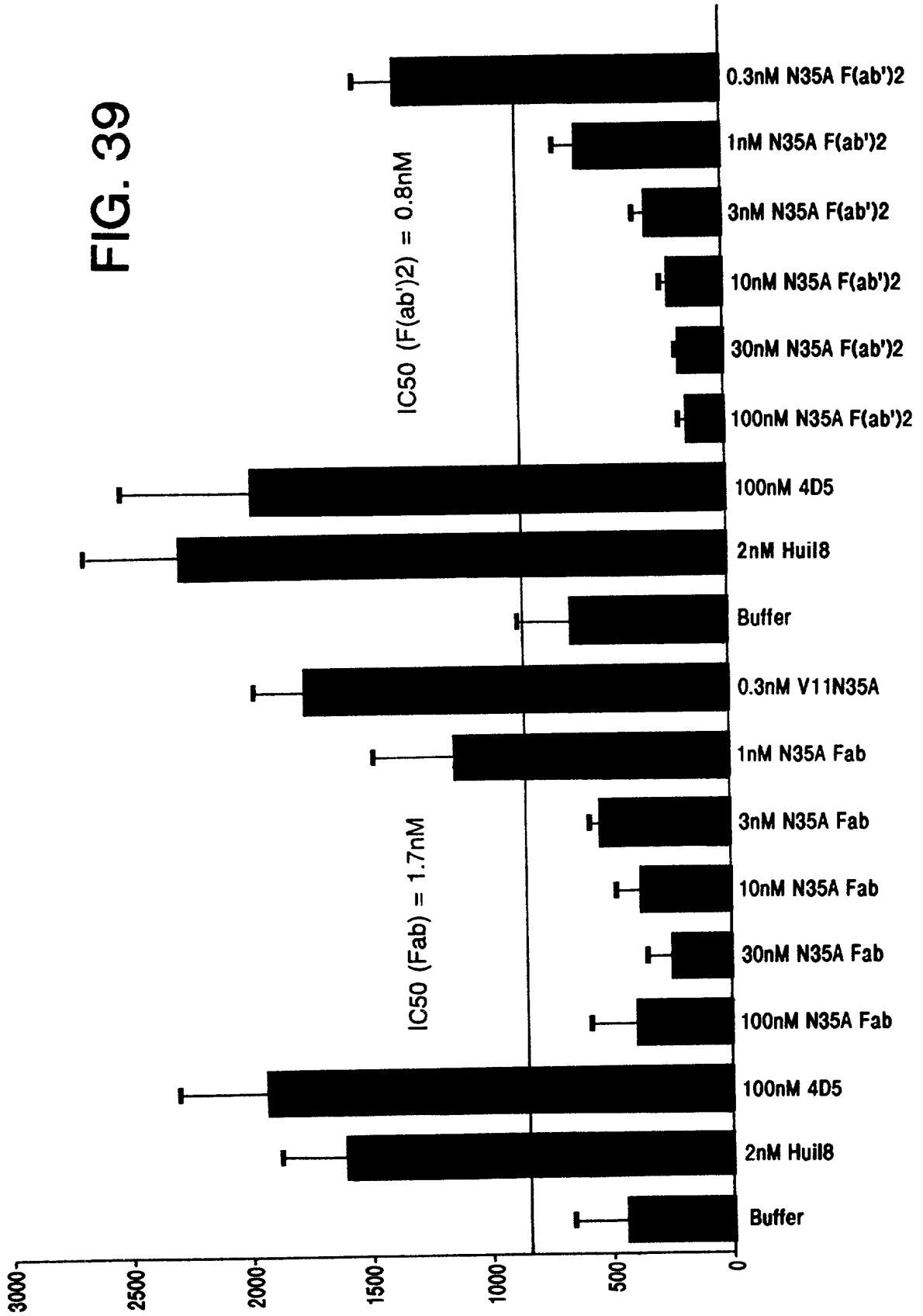
1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA
GAGTTTTTCG AACAGCCCCT CGCGATT
268 L K K L V G E R O

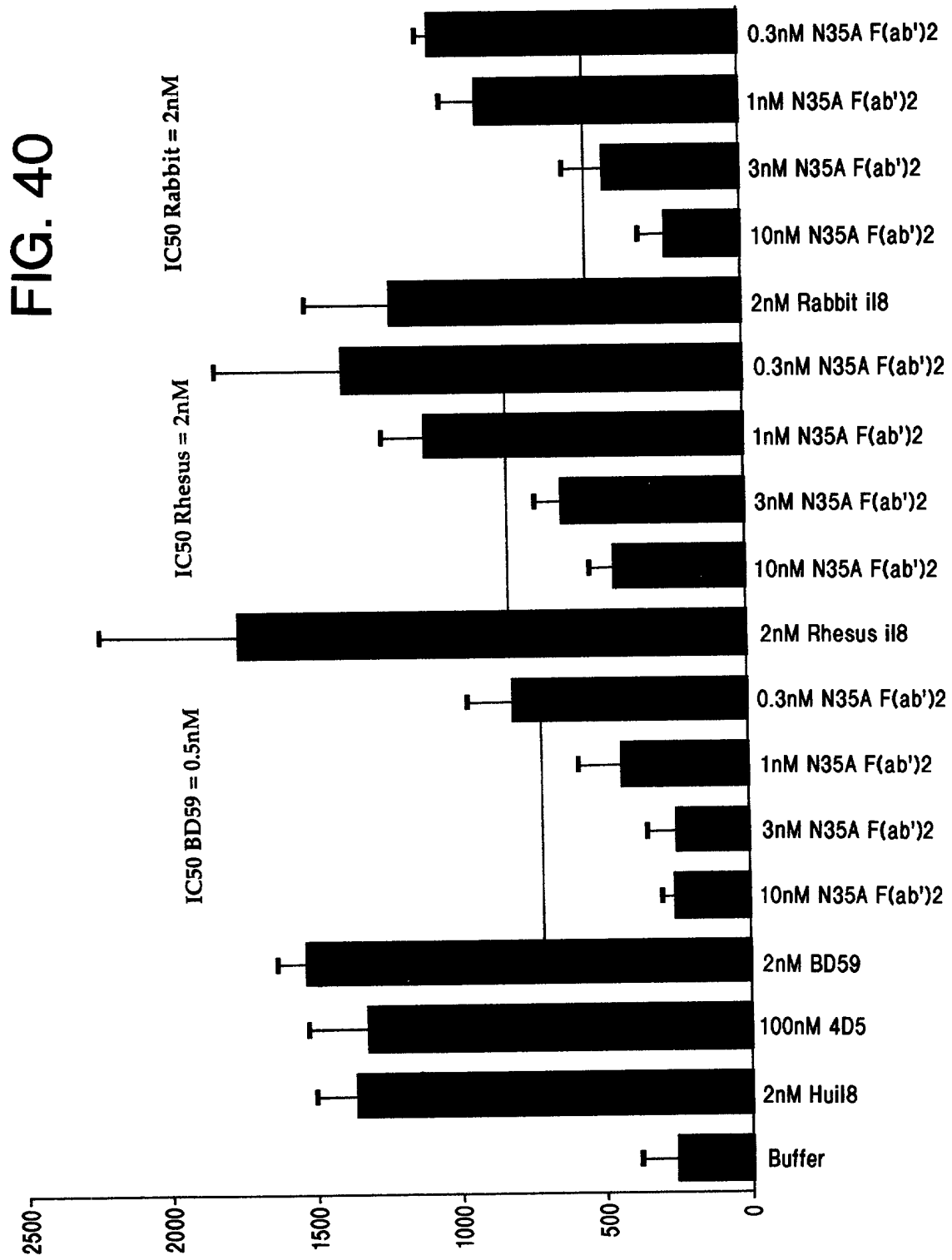
FIG. 37B



Cold Ligand (nM)

FIG. 38





[illegible]

FIG. 41A

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164 165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218 219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242 243 244 245 246 247 248 249 250 251 252 253 254 255 256 257 258 259 260 261 262 263 264 265 266 267 268 269 270 271 272 273 274 275 276 277 278 279 280 281 282 283 284 285 286 287 288 289 290 291 292 293 294 295 296 297 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 313 314 315 316 317 318 319 320 321 322 323 324 325 326 327 328 329 330 331 332 333 334 335 336 337 338 339 340 341 342 343 344 345 346 347 348 349 350 351 352 353 354 355 356 357 358 359 360 361 362 363 364 365 366 367 368 369 370 371 372 373 374 375 376 377 378 379 380 381 382 383 384 385 386 387 388 389 390 391 392 393 394 395 396 397 398 399 400 401 402 403 404 405 406 407 408 409 410 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425 426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442 443 444 445 446 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 470 471 472 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 491 492 493 494 495 496 497 498 499 500 501 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517 518 519 520 521 522 523 524 525 526 527 528 529 530 531 532 533 534 535 536 537 538 539 540 541 542 543 544 545 546 547 548 549 550 551 552 553 554 555 556 557 558 559 560 561 562 563 564 565 566 567 568 569 570 571 572 573 574 575 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 595 596 597 598 599 600 601 602 603 604 605 606 607 608 609 610 611 612 613 614 615 616 617 618 619 620 621 622 623 624 625 626 627 628 629 630 631 632 633 634 635 636 637 638 639 640 641 642 643 644 645 646 647 648 649 650 651 652 653 654 655 656 657 658 659 660 661 662 663 664 665 666 667 668 669 670 671 672 673 674 675 676 677 678 679 680 681 682 683 684 685 686 687 688 689 690 691 692 693 694 695 696 697 698 699 700 701 702 703 704 705 706 707 708 709 710 711 712 713 714 715 716 717 718 719 720 721 722 723 724 725 726 727 728 729 730 731 732 733 734 735 736 737 738 739 740 741 742 743 744 745 746 747 748 749 750 751 752 753 754 755 756 757 758 759 760 761 762 763 764 765 766 767 768 769 770 771 772 773 774 775 776 777 778 779 780 781 782 783 784 785 786 787 788 789 790 791 792 793 794 795 796 797 798 799 800 801 802 803 804 805 806 807 808 809 810 811 812 813 814 815 816 817 818 819 820 821 822 823 824 825 826 827 828 829 830 831 832 833 834 835 836 837 838 839 840 841 842 843 844 845 846 847 848 849 850 851 852 853 854 855 856 857 858 859 860 861 862 863 864 865 866 867 868 869 870 871 872 873 874 875 876 877 878 879 880 881 882 883 884 885 886 887 888 889 890 891 892 893 894 895 896 897 898 899 900 901 902 903 904 905 906 907 908 909 910 911 912 913 914 915 916 917 918 919 920 921 922 923 924 925 926 927 928 929 930 931 932 933 934 935 936 937 938 939 940 941 942 943 944 945 946 947 948 949 950 951 952 953 954 955 956 957 958 959 960 961 962 963 964 965 966 967 968 969 970 971 972 973 974 975 976 977 978 979 980 981 982 983 984 985 986 987 988 989 990 991 992 993 994 995 996 997 998 999 1000

```

scrFI
nciI
mspI
hpaII
dsav
xmaI/pspAI
smaI
scrFI
nciI
dsav
cauII
bsaJI
avaI
sau3AI taqI
rsaI mboI/ndeII[dam-]
csp6I dpnI[dam+]
nlaIV nlaIV paer7I
kpnI cauII dpnII[dam-]
hgiCI bstYI/xhoII
bani bsaJI alwI[dam-] hphI
asp718 bamHI avaI
acc65I alwI[dam-] mnlI mnlI
401 TCGGTACCCG GGGATCCTCT CGAGGTTGAG GTGATTTTAT GAAAAGAAT ATCGCATTTT TTCTTGCATC TATGTTTCGT TTTTCTATTG CTACAAACGC
ACCATGGGC CCTAGGAGA GCTCCAAC TC CACTAAAATA CTTTTCCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC GATGTTTGGC
M K K N I A F L L A S M F V F S I A T N A
a mutation was found that inactivated the mluI site. The penultimate nucleotide was changed fr G toT ^
-23

sstI
sacI
hgiJII
hgiAI/aspHI
ecII36II
bsp1286
bsiHKAI
bsmFI bmyI
bsrI avaI aluI
tth111I/aspI banII aciI
mnlI
ecoRV
501 ATACGCTGAT ATCCAGATGA CCCAGTCCCC GAGCTCCCTG TCCGCCCTCTG TGGCGCATAG GGTCAACATC ACCTGCAGGT CAAGTCAAAG CTTAGTACAT
TATGGCACTA TAGTCTACT GGGTCAGGGG CTCGAGGGAC AGCGGAGAC ACCCGCTATC CCAGTGGTAG TGGAGCTCCA GTTCAGTTTC GAATCATGTA
-2 Y A D I Q M T Q S P S S L S A S V G D R V T I T C R S S Q S L V H

```

FIG. 41B

```

scrFI      tfil
mvaI       hinfI      bsmFI
ecorII     taqI       bpmI/gsuI[dcM-]
dsav       clalI/bsp106 pleI
bstNI      bspDI[dam-] hinfI
apyI[dcM+]
601 GGTATAGGTG CTACTATTTT ACACGTGGTAT CAACAGAAAC CAGGAAAAGC TCCGAAACTA CTGATTTCAC AAGTATCCAA TCGATTCTCT GGAGTCCCCTT
CCATATCCAC GATGCATATAA TGTGACCATA GTTGCTTTTG GTCTTTTTCG AGCCTTTGAT GACTAAATGT TTCAVAGGTT AGCTAAGAGA CCTCAGGGAA
32 G I G A T Y L H W Y Q Q K P G K A P K L L I Y K V S N R F S G V P S

        bsrI
        mspI
        hpaII
        bslI
        bsaWI
        sau3AI
        mboI/ndeII[dam-]
        dpnI[dam+]
        dpnII[dam-]
        alwI[dam-]
        nlaIV
        bstYI/xhoII
        bamHI
        alwI[dam-] bsmFI
701 CTCGCTTCTC TGGATCCGGT TCTGGGACGG ATTTCACTCT GACCATCAGC AGTCTGCAGC CAGAAGACTT CGCAACTTAT TACTGTTTAC AGAGTACTCA
GAGCGAAGAG ACCTAGGCCA AGACCTTGCC TAAAGTGAGA CTGGTAGTCG TCAGACGTCG GTCTTCTGAA CGGTTGAATA ATGACAAGTG TCTCATGAGT
66 R F S G S G S G T D F T L T I S S L Q P E D F A T Y Y C S Q S T H

        styI
        bsaJI
        rsaI
        csp6I
        nlaIV
        kpnI
        hgiCI
        banI
        asp718
        acc65I
        maeII
        bsrBI
        aciI
        bsmFI
801 TGTCCCGCTC ACGTTTGGAC AGGTATCCAA GGTGGAGATC AAACGAACGTG TGGCTGCACC ATCTGTCTTC ATCTTCCGCG CATCTGATGA GCAGTTGAAA
ACAGGGCGAG TGCAAACCTG TCCCATGGTT CCACCTCTAG TTGCTTGAC ACCGACGTGG TAGACAGAAG TAGAAGGCGG GTAGACTACT CGTCAACTTT
99 V P L T F G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K

        mboII
        bpuAI
        bbsI
        mboII
        aciI

```

FIG. 41C

1001 AGGAGAGTGT CACAGAGCAG GACAGCAAGG ACAGCACCTA CAGCCTCAGC AGCACCTGA CGCTGAGCAA AGCAGACTAC GAGAAACACA AAGTCTACGC
 TCTCTCACA GTGTCCTCC CTGTCCTCC TGTCGTGGAT GTCGGAGTCG TCGTGGGACT GCAGCTCGT TCGTCTGATG CTCCTTGTGT TTCAGATGCG
 166 E S V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A

901 TCTGGAACG CTTCTGTGT GTGCTGCTG AATAACTTCT ATCCACAGAGA GGCCAAAGTA CAGTGAAGG TGGATAACGC CCTCCAATCG GGTAACCTCCC
 AGACCTTGAC GAAGACAACA CACGGACGAC TTATTGAAGA TAGGCTCTCT CCGGTTTCAT GTCACCTCC ACCTATTGCG GGAGGTTAGC CCATTGAGGG
 132 S G T A S V V C L L N N F Y P R E A K V Q W K V D N A L Q S G N S Q

1001 AGGAGAGTGT CACAGAGCAG GACAGCAAGG ACAGCACCTA CAGCCTCAGC AGCACCTGA CGCTGAGCAA AGCAGACTAC GAGAAACACA AAGTCTACGC
 TCTCTCACA GTGTCCTCC CTGTCCTCC TGTCGTGGAT GTCGGAGTCG TCGTGGGACT GCAGCTCGT TCGTCTGATG CTCCTTGTGT TTCAGATGCG
 166 E S V T E Q D S K D S T Y S L S S T L T L S K A D Y E K H K V Y A

1101 CTGCGAAGTC ACCCATCAGG GCCTGAGCTC GCCCGTCACA AAGAGCTTCA ACAGGGGAGA GTGTTAAGCT GATCTCTAC GCCGGACGCA TCGTGGCCCT
 GACGCTCAG TGGGTAGTCC CGGACTCGAG CGGGCAGTGT TTCTCGAGT TGTCCCTCT CACAATCGA CTAGGAGATG CGGCTCGCT AGCACCGGGA
 199 C E V T H Q G L S S P V T K S F N R G E C O

FIG. 41D

1201 AGTACGCAAC TAGTCGTAAA AAGGTATCT AGAGTTGAG GTGATTTAT GAAAAAGAA ATCGCATTC TTCTTGCATC TATGTTCGTT TTTTCTATTG
TCATGCGTTG ATCAGCATTT TTCCCATAGA TCtCCAACTC CACTAAATA CTTTtTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC
M K K N I A F L L A S M F V F S I A

1201
-23

1301 CTACAAACG GTACGCTGAG GTTCAGCTAG TGCAGTCTGG CGGTGGCTG GTGCAGCCAG GGGCTCACT CCGTTTGTCC TGTGCAGCTT CTGGCTACTC
GATGTTTGG CATGCGACTC CAAGTCGATC ACGTCAGACC GCCACGGAC CACGTCGGTC CCGCAGTGA GCGAAACAGG ACACGTCGAA GACCGATGAG
-5 T N A Y A E V Q L V Q S G G G L V Q P G G S L R L S C A S G Y S

1301

FIG. 41E

[illegible]

FIG. 41E

1701 ATCGGCTTTC CCCCTGGCAC CCTCCTCCAA GAGCACCTCT GGGGGCACAG CGGCCCTGGG CTGCCTGGT AAGGACTACT TCCCCGAACC GGTGACGGTG
 TAGCCAGAAG GGGGACCGTG GGAGGAGGTT CTCGTGGAGA CCCCGTGTC GCGGGACCC GACGGACCAG TTCCTGATGA AGGGGCTGG CCACTGCCAC
 129 S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P V T V

1801 TCGTGAACCT CAGGCGCCCT GACCAGCGGC GTGCACACCT TCCCGGCTGT CCTACAGTCC TCAGGACTCT ACTCCCTCAG CAGCGTGGTG ACCGTGCCCT
 AGCACTTGA GTCCGCGGGA CTGGTCGCGG CACGTGTGGA AGGGCCGACA GGATGTCAGG AGTCCTGAGA TGAGGGAGTC GTCGCACCAC TGGCACGGGA
 162 S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V T V P S

1901 CCAGCAGCTT GGGCACCCAG ACCTACATCT GCAACGTGAA TCACAAGCCC AGCAACACCA AGGTCGACAA GAAAGTTGAG CCCAATCTT GTGACAAAAC
 GGTCTCGAA CCCGTGGGTC TGGATGTAGA CGTTGCACTT AGTGTGCGG AGTGTGCGG TCGTGTGGT TCCAGTGT TTTCAACTC GGGTTAGAA CACTGTTTG
 196 S S L G T Q T Y I C N V N H K P S N T K V D K K V E P K S C D D K T

FIG. 41G


```
fnu4HI
bsoFI
haeIII/palI
mcrI
eagI/xmaIII/ecI XI
eaeI
cfrI
bsiEI
notI
fnu4HI
bsoFI nlaIII
aciI aciI aluI mnlI taqI aluI
rmaI
maeI
bfaI tthlII/aspI
sapi
mboII
earI/ksp632I
rmaI
maeI
bfaI
2001 TCACACATGC CCGCGTGCC CAGCACCAGA ACTGCTGGC GCGCGCATGA AACAGTAGA GGAAGAAGTC GAAGAGCTAC TCTCCAAGAA CTACCACCTA
AGTGTGTACG GCGGACACGG GTCGTGGTCT TGACGACCG CCGGGGTACT TTGTCGATCT CCTGTTCCAG CTCTCGATG AGAGGTTCTT GATGGTGGAT
229 H T C P C P A P E L L G G R M K Q L E D K V E E L L S K N Y H L
^junction between antibody and leucine zipper

scrFI
nciI
mspI
hpaII
dsav
cauII
aciI
fnu4HI
bsoFI
2101 GAGAATGAAG TGGCAAGACT CAAAAGCTT GTCGGGGAGC GCTAAGCATG CGACGGCCCT AGAGTCCCTA ACGCTCGGT GCCGCCGGC GTTTTTTATT
CTCTTACTTC ACCGTTCTGA GTTTTTCGAA CAGCCCTCG CGATTCGTAC GTCGCCGGA TCTCAGGGAT TCGAGCCAA CGCGGCCCG CAAAAAATAA
262 E N E V A R L K K L V G E R O

tru9I
mseI
hpaI nlaIII
hincII/hindII
2201 GTTAACATCT GTTTGACAGC TTATCATCGA TAAGCTTAA TCGGTAGTT TATCACAGTT AAATGCTAA CGCAGTCAGG CACCGTGTAT GAAATCTAAC
CAATTGAGTA CAAACTGTCG AATAGTAGCT ATTCGAAAT ACCCATCAA ATAGTGTCAA TTAAACGATT GCGTCAGTCC GTGGCACATA CTTAGATTG
```

FIG. 41H

2301 AATGGCTCA TCGTCATCCT CGGCACCGTC ACCCTGGATG CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TCGCGGCCT CTTGCGGGAT ATCGTCCATT
 TTACGGGAGT ACCAGTAGGA GCCGTGGCAG GCCGTGGCAG TGGGACCTAC GACATCCGTA TCGGAACCAA TACGGCCATG ACGGCCGGA GAACGCCCTA TAGCAGGTAA
 2401 CCGACAGCAT CGCCAGTCAC TATGGCGTGC TGCTAGCGCT ATATGCGTTG ATGCAATTTT TATGCGCACC CGTTCTCGGA GCACCTCTCCG ACCGCTTTGG
 GGCTGTCGTA GCGGTCACTG ATACCGCAGC ACGATCGCGA TATACGCAAC TAGGTTAAAG ATACGCGTGG GCAAGACCT CGTGACAGGC TGGCGAAACC
 2501 CCGCGGCCCA GTCCTGCTCG CTTGCGTACT TGGAGCCACT ATCGACTACG CGATCATGGC GACCACACC GTCCCTGTGA TCCTCTACGC CGGACGCATC
 GGCGGCGGT CAGGACGAGC GAAGCGATGA ACCTCGGTGA TAGCTGATGC GGTAGTACCG CTGGTGTGG CAGGACACCT AGGAGATCG GCCTGCGTAG

FIG. 41I

hinPI
 hhaI/cfoI
 nlaIV
 nari
 kasi
 hinII/acyI
 hgiCI
 haeII
 mspI
 hpaII
 nael
 cfrI01/bsrFI bani
 cac8I sgrAI
 haeIII/pali hpaII
 eaeI hphi ahaII/bsaHI
 cfrI sfaNI cfrI01/bsrFI acII cac8I
 2601 GTGGCCGGCA TCACCGCGC CACAGGTGCG GTTGCTGGCG CCTATATCGC CGACATCACC GATGGGGAAG ATCGGGCTCG CCACCTTCGG CTCATGACGC
 CACCGGCCGT AGTGGCCGCG GTGTCCACGC CAACGACCGC GGATATAGCG GCTGTAGTGG CTACCCCTTC TAGCCCGAGC GGTGAAGCCC GAGTACTCGC
 hinPI
 hhaI/cfoI
 nlaIV
 nari
 kasi
 hinII/acyI
 hgiCI
 haeII
 bani
 ahaII/bsaHI
 cac8I
 hphi
 mboII[dam-]
 hgiJII
 bsp1286
 bmyI
 banII
 sau3AI cac8I
 mboI/ndeII[dam-]
 dpnI[dam+]
 dpnII[dam-]
 mboII[dam-]
 hgiJII
 haeII
 bsp1286
 eco47III
 bmyI bspHI hhaI/cfoI
 banII nlaII
 rcaI hinPI
 scrFI
 nciI
 mspI
 hpaII
 dsal
 bsII
 cauII
 sau96I
 nlaIV
 eaeI
 haeIII/pali
 asuI bsaJI bsaJI
 eco0109I/draII
 cac8I bsII cfrI bsmFI
 2701 CTTGTTTCGG CTGGGGTATG GTGGCAGGCC CCGTGCCCGG GGGACTGTGG GGCGCCATCT CCTTGCAAGC ACCATTCTT CGCGCGCGCG TGCTCAACGG
 GAACAAAGCC GCACCCATAC CACCGTCCGG GGCACCGGCC CCCTGACAAC CCGCGGTAGA GGAACGTGG TGGTAAGGAA CGCCGCCGCC ACAGTTGCC
 fnu4HI
 bsoFI
 bsri bsvI
 bsII
 pleI
 hinfi
 hgaI
 sfaNI
 bsaWI
 bsri aluI bsII
 haeIII/pali
 mspI
 hpaII
 bsaWI
 2801 CCTCAACCTA CTACTGGGCT GCTTCCTAAT GCAGGAGTCG CATAGGGAG AGCGTCGTCC GATGCCCTTG AGAGCCTTCA ACCCAGTCAG CTCTTCCGG
 GGAGTTGGAT GATGACCCGA CGAAGGATTA CGTCTCTCAGC GTATTCCCTC TCGCAGCAGG CTACGGGAAC TCTCGGAAGT TGGGTCAGTC GAGGAAGGCC

FIG. 41J

[illegible]

FIG. 41L

hphI hhaI/cfoI hinPI hgaI
tfII pflMI mstI pflMI hhaI/cfoI
hinFI bslI bsmI avIII/fspI styI bsh1236I
acII bsmI bslI bsajI
nlaIV
3501 CTAACGGATT CACCACTCCA AGAATTGGAG CCAATCAATT CTTGCGGAGA ACTGTGAATG CGCAACCAA CCCTTGGCAG AACATATCCA TCGCCGTCCGC
GATTGCCATA GTGGTGAGGT TCTTAACCTC GGTTAGTTAA GAACGCCTCT TGACACTTAC GCGTTTGGTT GGAACCGTC TTGTATAGGT AGCGCAGGCG

haeIII/palI mspI
mscI/balI hpaII
haeI scrFI nciI
scrFI mvaI dsal ecorII dsav
bstNI
bslI bsajI sau3AI mboI/ndeII[dam-] nlaIV
apyI[dcM+] sau96I dpnI[dam+] avaiI cac8I
sau96I avaiI hinPI dpnII[dam-] asuI rmaI
asuI eaeI hhaI/cfoI hgiAI/asphI ppuMI maeI
ppuMI mstI nlaIII bsp1286
nlaIV cfrI avIII/fspI bsiHKAI mnlI caulI-bfaI acII
eco0109I/draII bmyI
bpmI/gsuI[dcM-] acII sfaNI
3601 CATCTCCAGC AGCCGCACGC GCGCATCTC GGGCAGCGTT GGGTCTCGGC CACGGGTGCG CATGATCGTG CTCCTGTCTG TGAGGACCG GCTAGGCTGG
GTAGAGGTCG TCGGCGTGCG CCGGTAGAG CCCGTCGCAA CCCAGGACCG GTGCCACGC GTACTAGCAC GAGGACAGCA ACTCCTGGGC CGATCCGACC

fnu4HI
thai hinPI
fnu4HI bsoFI
bsoFI fnuDII/mvni
fnu4HI bstUI
bsoFI cac8I hhaI/cfoI fnu4HI fnu4HI
bbvI acII bsh1236I avaI bsoFI bbvI
bpmI/gsuI[dcM-] acII sfaNI
3601 CATCTCCAGC AGCCGCACGC GCGCATCTC GGGCAGCGTT GGGTCTCGGC CACGGGTGCG CATGATCGTG CTCCTGTCTG TGAGGACCG GCTAGGCTGG
GTAGAGGTCG TCGGCGTGCG CCGGTAGAG CCCGTCGCAA CCCAGGACCG GTGCCACGC GTACTAGCAC GAGGACAGCA ACTCCTGGGC CGATCCGACC

fnu4HI
cac8I
thai
fnuDII/mvni
bstUI
hphI
tfII
hinFI
bsh1236I
maeII
bbvI
bsoFI
fnu4HI
bbvI
maeII
dclI
nlaIII
3701 CGGGGTGCC TTAATGGTTA GCAGAATGAA TCACCGATAC GCGAGCGAAC GTGAGCGCAC TGCTGCTGCA AAACGTCTGC GACCTGAGCA ACAACATGAA
GCCCAACGG AATGACCAAT CGTCTTACTT AGTGGCTATG CGCTCGGTG CACTCGCTG ACAGCAGCGT TTTGCAGACG CTGGACTCGT TGTGTACTT

FIG. 41M

sau3AI
mboI/ndeII[dam-]
mamI[dam-]
dpmI[dam+]
dpmII[dam-]
bstYI/xhoII
alwI[dam-]
mspI
hpaII
mroI bsaBI[dam-] fnu4HI
bspMI
bspEI[dam-] bsoFI
bsaWI sfanI bbvI
accII[dam-] sfanI
foki cac8I
TTATGTTCCG GATCTGCATC GCAGGATGCT GCTGGTACC
CGTCCCTACGA CGACCGATGG
3801
ACCGAAGCC
TTTCCGTGTT TCGTAAAGTC TGGAAACGGC GAAGTCAGCG CCCTGCACCA
TTATGTTCCG GATCTGCATC GCAGGATGCT GCTGGTACC
CGTCCCTACGA CGACCGATGG
3901
GACACCTTGT GGATGTAGAC ATAATTGCTT CGCAGCCGTA ACTGGGACTC
ACTAAAGA GACCGAGGCG GCGTAGGTAT GCGGTCAAC AAATGGGAGT
TTTACCTCTCA
4001
GTTGCAAGGT CATTGGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC
GTAGGAGAGA GCAAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG
TTTACCTCTCA

FIG. 41N

[illegible]

FIG. 410

[illegible]

FIG. 41P

4801 GAAACCCGAC AGGACTATAA AGATACCAGG CGTTTCCCCC TGGAGCTCC CTCGTGCGCT CTCCTGTCTCC GACCTGCGG CTTACCGGAT ACCTGTCCGC
 CTTTGGGCTG TCTATGATATT TCTATGGTCC GCAAGGGGG ACCTTCGAG GAGCACGGA GAGGACAAGG CTGGGACGGC GAATGCGCTA TGGACAGGCG

scrFI

scrFI mvaI

mvaI ecorII

ecorII dsav

dsav bstNI

bstNI hinPI

apyI[dcM+] bsaJI aluI mnlI hhaI/cfoI

bslI

4801 GAAACCCGAC AGGACTATAA AGATACCAGG CGTTTCCCCC TGGAGCTCC CTCGTGCGCT CTCCTGTCTCC GACCTGCGG CTTACCGGAT ACCTGTCCGC
 CTTTGGGCTG TCTATGATATT TCTATGGTCC GCAAGGGGG ACCTTCGAG GAGCACGGA GAGGACAAGG CTGGGACGGC GAATGCGCTA TGGACAGGCG

hgiAI/aspHI
 bsp1286

bsiHKA

bmyI

apaLI/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

alw44I/snoI

FIG. 41Q

```

mspI
hpaII
sau3AI
mboI/ndeII[dam-]
dpnI[dam+]
dpnII[dam-]
alwI[dam-]
maeIII
eco57I bsrI
TCTGCTGAAG CCAGTTACCT TCGGAAAAAG AGTTGGTAGC TCCTGATCCG GCAAAACAAAC CACCGCTGGT AGCGGTGGTT TTTTGTGTTG CAAGCAGCAG
AGACGACTTC GGTCAATGGA AGCCTTTTTC TCAACCATCG AGAACATAGG CGTTGTGTTG GTGGCGACCA TCGCCACCAA AAAACAAAC GTTCGTCGTC
                    aluI
                    nspBII
                    aciI
                    cac8I
                    fnu4HI
                    bsoFI
                    bbvI
                    5201

                    sau3AI
                    mboI/ndeII[dam-]
                    mboI/ndeII[dam-]
                    sau3AI mboII[dam-] dpnI[dam+]
                    mboI/ndeII[dam-] dpnII[dam-]
                    dpnI[dam+] dpnI[dam+]
                    dpnII[dam-] dpnII[dam-]
                    bstYI/xhoII alwI[dam-]
                    alwI[dam-] bstYI/xhoII
                    bsh1236I
                    5301 ATTACGCGCA GAAAAAAGG ATCTCAAGAA GATCCCTTTGA TCCTTTTCTAC GGGGTCTGAC GCTCAGTGGA ACGAAAACTC ACGTTAAGG ATTTTGGTCA
                    TAATGGCGGT CTTTTTTTCC TAGAGTTCTT CTAGGAAACT AGAAAAAGATG CCCAGACTG CGAGTCACCT TGCTTTTGAG TGCAATTCCC TAAACCCAGT
                    tru9I
                    mseI
                    maeII
                    nlaIII
                    rcaI
                    bspHI
                    hgaI ddeI
                    5401 TGAGATTATC AAAAAGGATC TTCACCTAGA TCCTTTTAAA TTAATAATGA AGTTTAAAT CAATCTAAAG TATATATGAG TAAACTTGGT CTGACAGTTA
                    ACTCTAATAG TTTTTCCTAG AAGTGGATCT AGGAAATTT AATTTTACT TCATAAATTTA GTTAGATTTC ATATATACTC ATTTGAACCA GACTGTCAAT
                    maeIII
                    nlaIV
                    hgiCI
                    bani
                    mnlI
                    tru9I
                    mseI
                    sau3AI
                    mboI/ndeII[dam-]
                    dpnI[dam+]
                    dpnII[dam-]
                    ddeI
                    foki
                    ahdI/eam1105I
                    pleI
                    hinfi
                    5501 CCAATGCTTA ATCAGTGAGG CACCTATCTC AGCGATCTGT CTATTTCGTT CATCCATAGT TGCCTGACTC CCGTCGCTGT AGATAACTAC GATACGGGAG
                    GGTACGAAT TACTCACCTCC GTGGATAGAG TCGCTAGACA GATAAGCAA GATAGATCA ACGGACTGAG GGGCAGCACA TCTATTGATG CTATGCCCTC
                    mnlI

```

[illegible]

FIG. 41S

6001 ATTTCTTTAC TGTCAATGCCA TCCGTAAGAT GCTTTTCTGT GACTGGTGAG TACTCAACCA AGTCATTCTG AGAATAGTGT ATGCGGCGGAC CGAGTTGCTC
TAAGAGAAATG ACAGTACGGT AGGCATTCTA CGAAAGACA CTGACCACTC ATGAGTTGGT TCAGTAAGAC TCTTATCACA TACGCCGCTG GCTCAACGAG

6001 ATTTCTTTAC TGTCAATGCCA TCCGTAAGAT GCTTTTCTGT GACTGGTGAG TACTCAACCA AGTCATTCTG AGAATAGTGT ATGCGGCGGAC CGAGTTGCTC
TAAGAGAAATG ACAGTACGGT AGGCATTCTA CGAAAGACA CTGACCACTC ATGAGTTGGT TCAGTAAGAC TCTTATCACA TACGCCGCTG GCTCAACGAG

6201 TTACCGCTGT TGAGATCCAG TTCGATGTAA CCCACTCGTG CACCCTCGTG ATCTTCAGCA TCCTTTACTT TCACCAGCGT TTCTGGGTGA GCAAAAACAG
AATGGCGACA ACTCTAGTC AAGCTACATT GGGTGAGCAC GTGGTTGAC TAGAAGTCGT AGAAATGAA AGTGGTCGCA AAGACCCACT CGTTTTTGTC

6301 GAAGGCAAAA TGCCGCAAAA AAGGGAATAA GGGCGACACG GAAATGTTGA ATACTCATAC TCCTCCTTTT TCAATATTAT TGAAGCATTT ATCAGGGTTA
CTTCCGTTTT ACGGCGTTTT TTCCCTTATT CCGCTGTGC CTTTACAACT TATGATATG AGAAGAAAA AGTTATAATA ACTTCGTAAA TAGTCCCAAT

FIG. 41T

hinPI
 thal
 fnuDII/mvt
 bstUI
 bsh1236I
 acil
 nlaIV hhal/cf
 nlaIII
 rcal
 bspHI acil
 bsmAI bsrBI
 6401 TTGTCTCATG AGCGGATACA TATTGGAATG TATTAGAAA AATAAACAAA TAGGGTTCC GCGACAA
 AACAGAGTAC TCGCCTATGT ATAACTTAC ATAAATCTTT TTATTGTTT ATCCCCAAGG CGCGTGTT
 sau96I
 haeIII/palI
 asuI mboII
 ecoO109I/draII
 mnli bpuAI
 bssSI
 nlaIII
 rcal tru9I
 bspHI msei
 6501 ACCATTATTA TCATGACATT AACCTATAAA AATAGGCGTA TCACGAGGCC CTTTCGTCTT CAA
 TGGTAATAAT AGTACTGTAA TTGGATATTT TTATCCGCAT AGTGTCCGG GAAAGCAGAA GTT

FIG. 41U

```
>length: 6563

aatII(GACGTC): 1645 6489
acc65I(GGTACC): 403 823
accI(GTMKAC): 1093 1963 4449
accIII(TCCGGA): 3867[dam-]
aciI(CCGC): 178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
acyI see hinII
aflIII(ACRYGT): 1307 4678
ageI(ACGGT): 1788
ahaII/bsaHI(GRCGYC): 1645 1813 2616 2637 2751 3408 6107 6489
ahaIII/draI(TTTAAA): 5435 5454 6146
ahdI/eam1105I(GACNNNNNGTC): 346 5566
aluI(AGCT): 72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
5922
alw44I/snoI(GTGCAC): 1831 4494 4992 6238
alwI[dam-](GGATC): 412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
6196 6214
alwNI[dcm-](CAGNNNCTG): 1117 1385 5089
apaI(GGGCCC): 1695
apalI/snoI(GTGCAC): 1831 4494 4992 6238
apoI(RAATTY): 1 391 4093
apyI[dcm+](CCWGG): 640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
aseI/asnI/vspI(ATTAAAT): 5742
asnI see aseI
asp700(GAANNNTTC): 905 930 4234 6166
asp718(GGTACC): 403 823
aspHI see hgiAI
aspi see tth111I
asuI(GGNCC): 1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463
```

FIG. 41V

Stop Template Primer

SL.97.2 5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3'

NNS Randomization Primer

SL.97.3 5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3'

FIG. 42

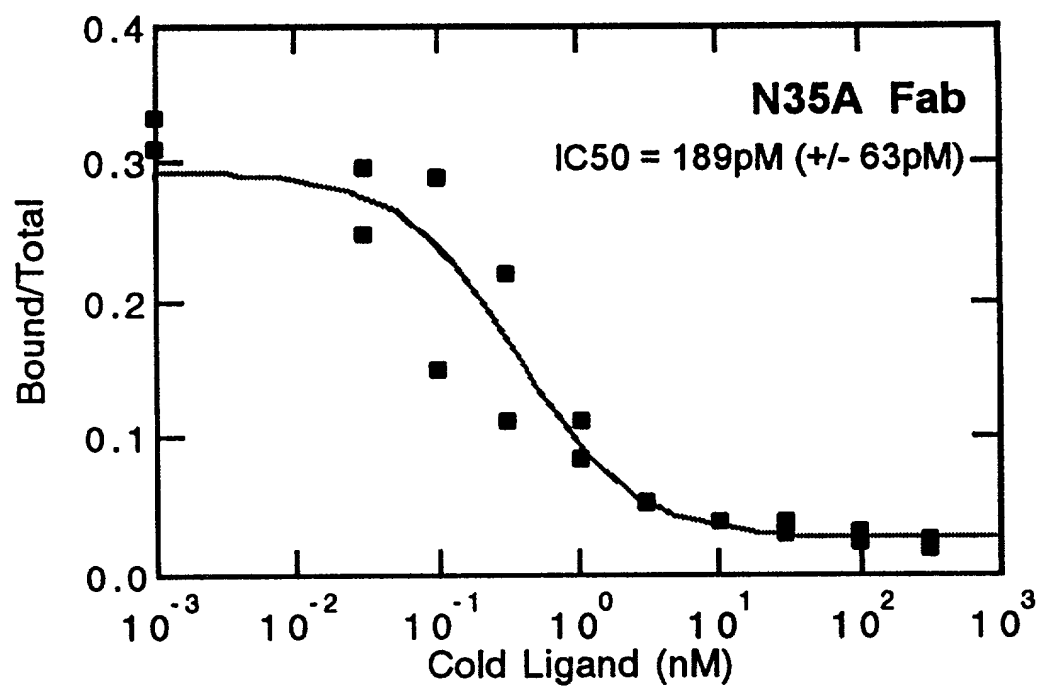


FIG. 43B

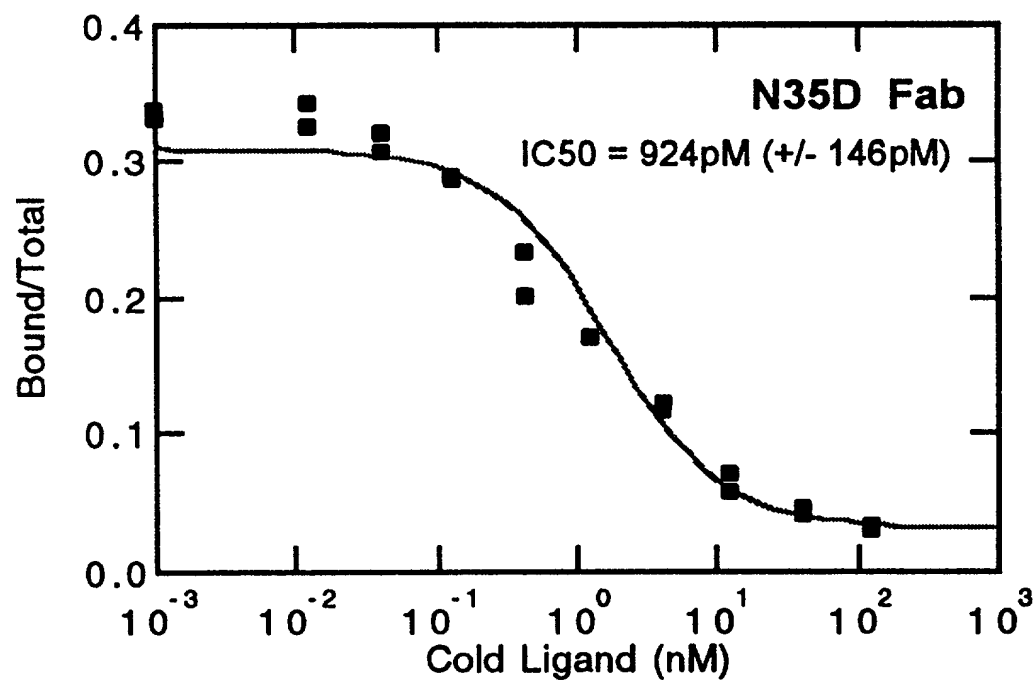


FIG. 43C

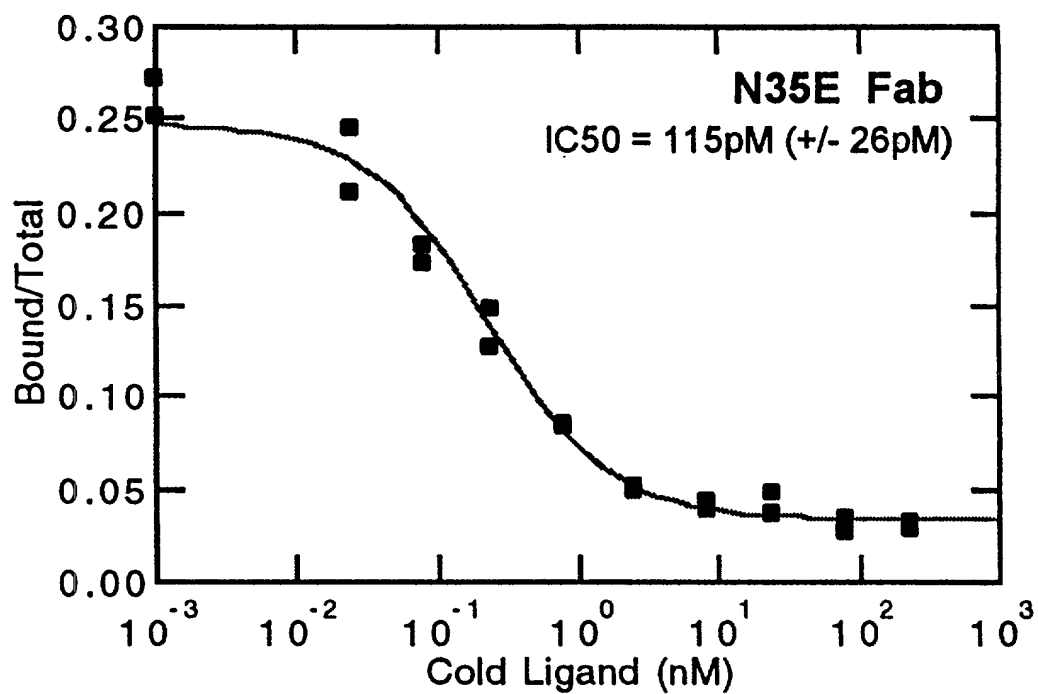


FIG. 43D

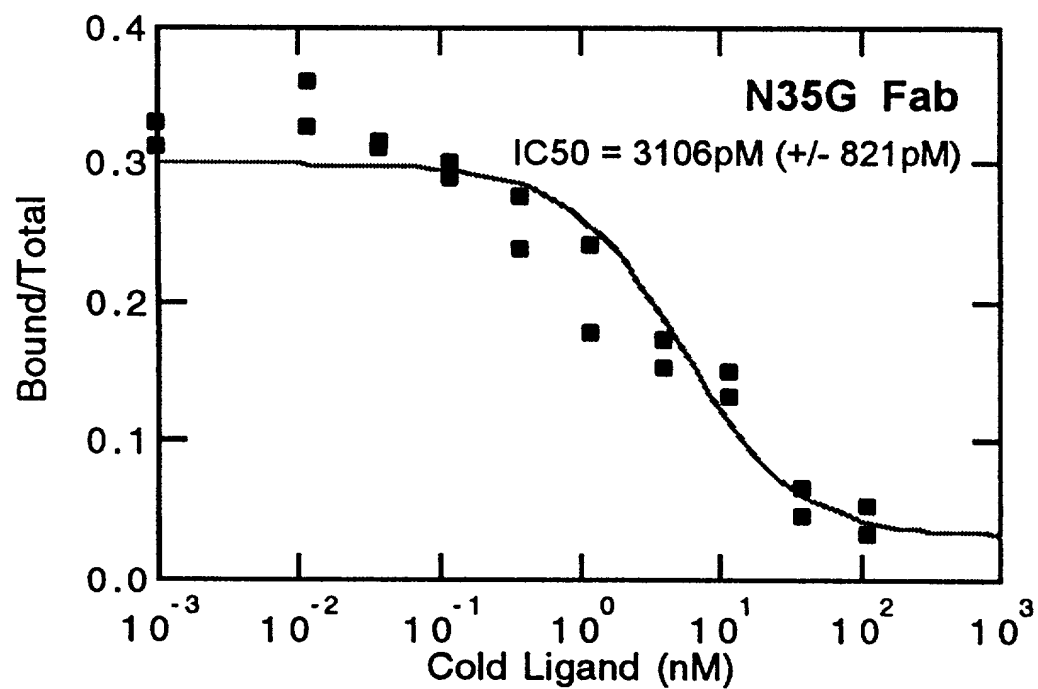
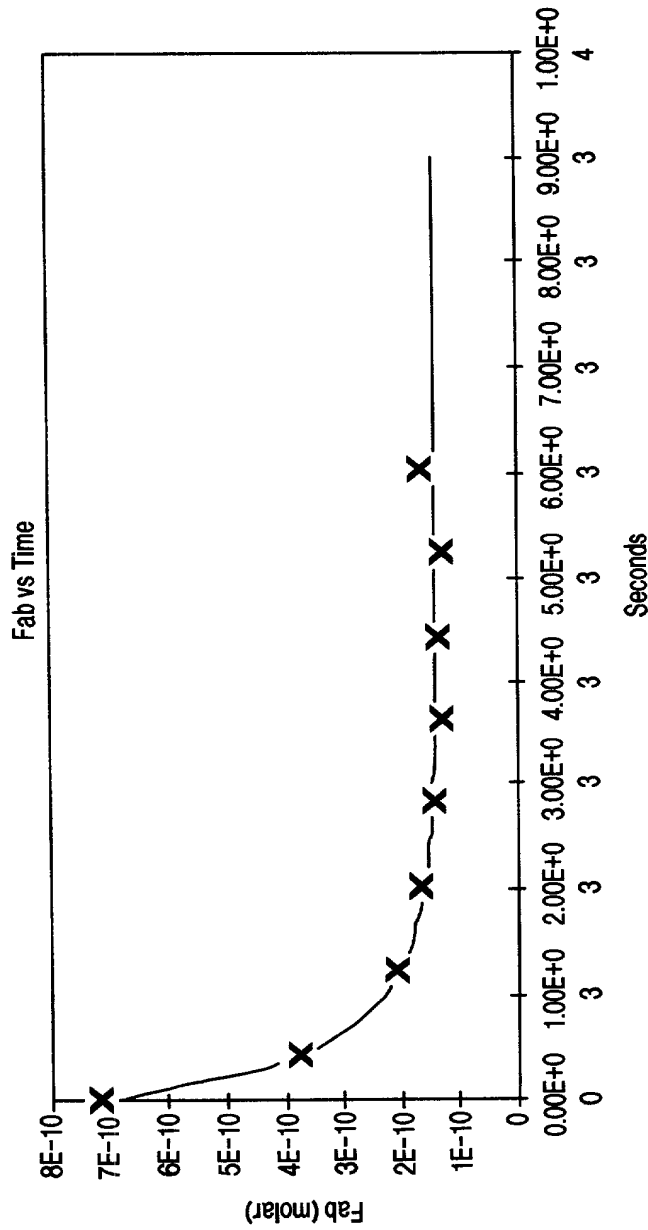


FIG. 43E



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')₂.

SAMPLE	ka	kd	Kd
6G4V11N35A-Fab	ND	ND	114pM
6G4V11N35A-F(ab') ₂	2.0x10 ⁶	2.1x10 ⁻⁴	109pM
6G4V11N35E-Fab	4.7x10 ⁶	2.6x10 ⁻⁴	54pM

FIG. 44

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
 TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
 -23 M K K N I A F L L A S M F V F S I A T N

 61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
 CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
 -3 A Y A D I Q M T Q S P S S L S A S V G D

 121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGAGACGTAT
 TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACTCTGCATA
 18 R V T I T C R S S O S L V H G I G E T Y

 181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
 AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
 38 L H W Y Q Q K P G K A P K L L I Y K V S

 241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
 TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
 58 N R F S G V P S R F S G S G S G T D F T

 301 CTGACCATCA GCAGCTTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
 GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
 78 L T I S S L Q P E D F A T Y Y C S O S T

 361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
 GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
 98 H V P L T F G Q G T K V E I K R T V A A

 421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
 GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
 118 P S V F I F P P S D E Q L K S G T A S V

 481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
 CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
 138 V C L L N N F Y P R E A K V Q W K V D N

 541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
 CGGGAGGTTA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCGTGG
 158 A L Q S G N S Q E S V T E Q D S K D S T

 601 TACAGCCTCA GCAGCACCCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
 ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
 178 Y S L S S T L T L S K A D Y E K H K V Y

 661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
 CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTCTCGAA GTTGTCCCCT
 198 A C E V T H Q G L S S P V T K S F N R G

 721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
 CTCACAATTC GACTAGGAGA TCGCGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
 218 E C O

FIG. 45

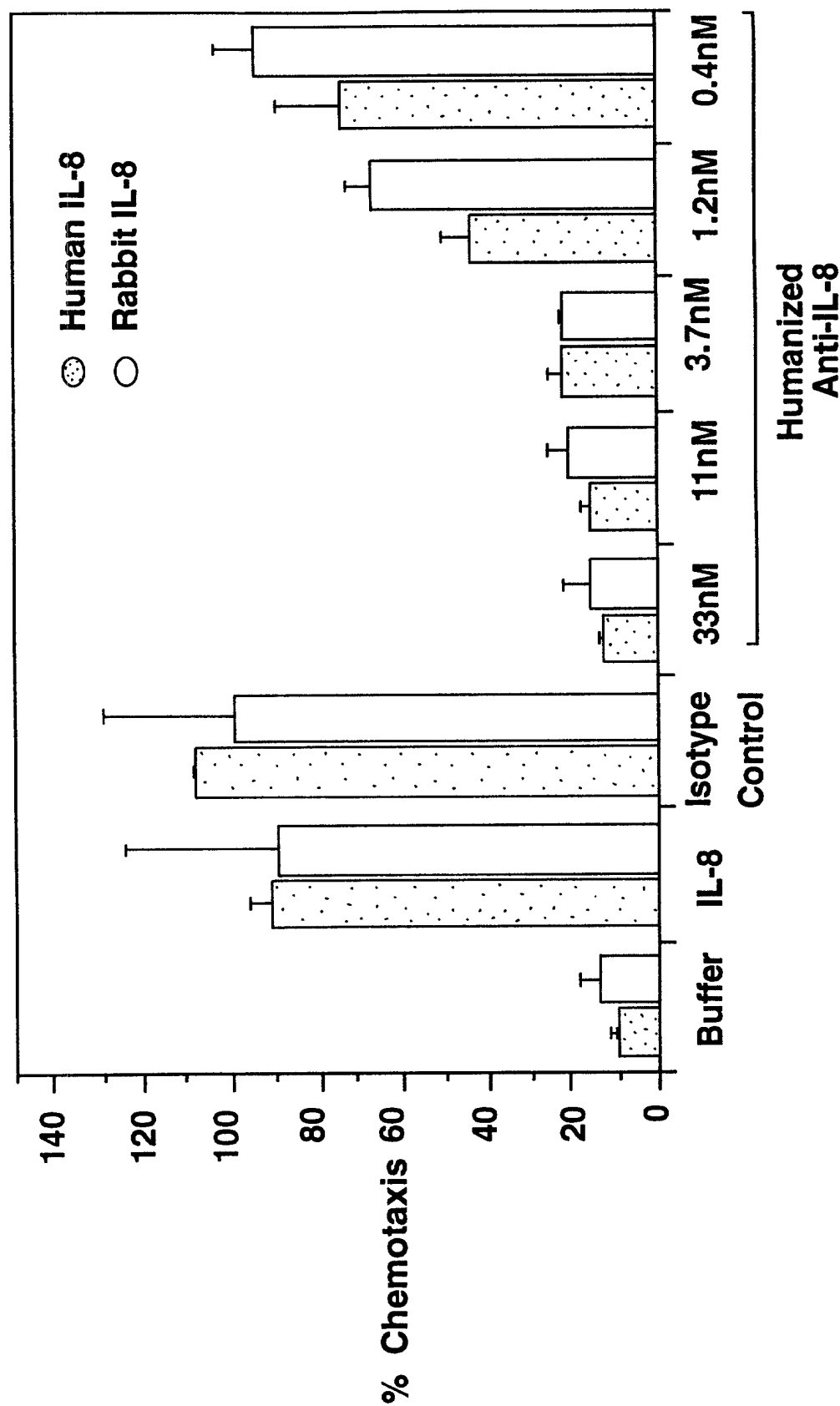


FIG. 46

N35AH1upr

5'-CTAGTGCAGTCTGGCGGTGGCCCTGGTGCAGCCAGGGGGCTCACTCCGTTTGTCCCTGTGCAGCTTCTGGCTACTCCTTC-3'

N35AH1lwr

5'-TCGAGAAGGAGTAGCCAGAAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAGGCCACCCGACACTGCACCT
AG-3'

Bold indicates nucleotide change destroying PvuII site.

FIG. 47

```

> Wed May 7 18:27:36 1997
> /home/ruby/vc/Immbio/afan/ss.p6G425v11.N35A.choSD
> sites: std
> length: 8120 (circular)
> This has the pSVI backbone with the pRK7 cloning linker (pSVI7) and the intron DHFR(ID)
> made from pSVI.WTSD.D by adding a linearization linker(LL) into the HpaI site

      cac8I
      aluI
      sstI
      sacI
      hgiI
      hgiAI/aspHI
      eclI36II
      bspI286
      bsiHKAI
      bmyI
      banII
      taqI
1  TTGCGAGCTCG CCCGACATTG ATTATTGACT AGAGTCGATC GACAGCTGTG GAATCTGTGT CAGTTAGGGT GTGGAAGATC CCCAGGCTCC CCAGCAGGCA
   AGACTCGAGC GGGCTGTAAC TAATAACTGA TCTCAGCTAG CTGTCGACAC CTTACACACA GTCAATCCCA CACCTTTCAG GGTCCGAGG GGTGCTCCGT

      scrFI
      mvaI
      ecorII
      dsav
      bstNI
      apyI[dcM+]
      bsaJI
      bsmFI
      nlaIV
      cac8I
      ppu10I
      nsII/avaIII
      nlaIII
      sphi
      nspI
      nspHI
      cac8I
101 GAAGTATGCA AAGCATGCAT CTCAATTAGT CAGCAACCGC GTGTGGAAAG TCCCAGGCT CCCGAGCAGG CAGAACTATG CAAGCATGC ATCTCAATTA
   CTTCAATACGT TTCGTACGTA GAGTTAATCA GTCGTTGGTC CACACCTTTC AGGGTCCGA GGGGTCTGCC GGGGTCTGCC GTCTTCAATC GTTTCGTACG TAGAGTTAAT

      nlaIII
      styI
      ncoI
      bslI
      dsal
      aciI
      bsaJI
      aciI
      bsrI
      aciI
201 GTCAACAACC ATAGTCCCGC CCTTAACCTCC GCCCATCCCG CCCCTAATCT CGCCAGTTC CGCCCATTTCT CGCCCATTCG GCGCCCATAG GCTGACTAAT TTTTTTTATT
   CAGTCGTTGG TATCAGGGCG GGGATTGAGG CGGGTAGGGC GGGGATTGAG GCGGTTCAAG GCGGGTAAGA GCGGGGTAC CGACTGATTA AAAAAAATAA

```

FIG. 48A

123456789101112131415161718192021222324252627282930313233343536373839404142434445464748495051525354555657585960616263646566676869707172737475767778798081828384858687888990919293949596979899100
 123456789101112131415161718192021222324252627282930313233343536373839404142434445464748495051525354555657585960616263646566676869707172737475767778798081828384858687888990919293949596979899100
 123456789101112131415161718192021222324252627282930313233343536373839404142434445464748495051525354555657585960616263646566676869707172737475767778798081828384858687888990919293949596979899100

```

      rmaI      maeI      haeIII/palI
      maeI      styI      mcrI
      bsaJI      blnI      eagI/xmaIII/ecI XI
      avrII[dam-]      rmaI      aluI
      haeIII/palI      maeI      maeI
      stuI      bfaI      cfrI
      haeI      nheI      bsiEI
      mnli      cac8I      mspI
      mnli bfaI      aluI      hpaII
      bseRI      TTTGGAGGCC TAGGCTTTTG CAAAAAGCTA GCTTATCCGG
301 TATGCAGAGG CCGAGGCCG CTCGGCCTCT GAGCTATTCC AGAAGTAGTG AGGAGGCTTT TTTGGAGGCC TAGGCTTTTG CAAAAAGCTA GCTTATCCGG
      ATACGTCCTC GGCTCCGGCG GAGCCGGAGA CTCGATAAGG TCTTCATCAC TCCTCCGAAA AAACCTCCGG ATCCGAAAAC GTTTTTCGAT CGAATAGGCC

      tfII      fnu4HI
      hinFI      bsoFI
      aciI      bbvI
      thaI      nspBII
      fnuDII/mvni      mnli      nlaIII
      bstUI      maeII      aciI
      bsh1236I      maeIII      csp6I      scfI
      CGGGAACGG TGCATTGGAA CGCGGATTCC CCGTGCCAAG AGTGACGTAA GTACCGCCTA TAGAGCGATA AGAGGATTTT ATCCCGCTG CCATCATGCT
401 GCGCCTTGCC ACGTAACCTT GCGCCTAAGG GGCACGGTTC TCACTGCATT CATGGCGGAT ATCTCGCTAT TCTCCTAAAA TAGGGCGGAC GGTAATACCA
      DHFR ATG^

      haeIII/palI
      haeI
      scrFI      bsrBI
      mvaI      ecorII
      dsav      bstNI      aciI
      pflMI      bsmAI      xmnI
      bslI      bsaI      asp700
      bsmFI      bsaJI      ddeI      scaI
      sfanI      GGGATTGGCA AGAACGGAGA CCTACCGTG CCTCCGCTCA GGAACGAGTT CAAGTACTTC
501 TCGACCATTC AACTGCATCG TCGCCGTGTC CCAAAATATG GGGATTGGCA AGAACGGAGA CCTACCGTG CCTCCGCTCA GGAACGAGTT CAAGTACTTC
      AGCTGGTAAC TTGACGTAGC AGCGGCACAG GGTTTTATAC CCCTAACCGT TCTTGCCTCT GGATGGACC GGAGCGAGT CCTTGCTCAA GTTCATGAAG

```

FIG. 48B

601 CAAAGAATCA CCACAACCTC TTCAGTGGAA GGTAACACAGA ATCTGGTGAT TATGGGTAGG AAAACCTGGT TCTCCATTCC TGAGAAGAAAT CGACCTTTAA
GTTTCTTACT GGTGTGGAG AAGTCACCTT CCATTGTCT TAGACCACTA ATACCCATCC TTTTGGACCA AGAGSTAAGG ACTCTTCTTA GCTGGAAATT

701 AGGACAGAAT TAATATAGTT CTCAGTAGAG AACTCAAAGA ACCACACGA GGAGCTCAAT TTCTTGCCAA AAGTTTGGAT GATGCCTTAA GACTTATTGA
TCCTGTCTTA ATTATATCAA GAGTCATCTC TTGAGTTTCT TGGTGGTGCT CCTCGAGTAA AAGAACGGTT TTCAAACCTA CTACGGAATT CTGAATAACT

801 ACAACCGGAA TTGGCAAGTA AAGTAGACAT GGTTTGGATA GTCGGAGGCA GTTCTGTGTTA CCAGGAAGCC ATGAATCAAC CAGGCCACCT TAGACTCTTT
TGTTGGCCTT AACCGTTTAT TTCATCTGTA CCAACCTAT CAGCCTCCGT CAAGACAAAT GGTCCTTCGG TACTTACTTG GTCGGTGA ATCTGAGAAA

FIG. 48C

```

hgai
hinli/acyl
ahali/bsaHI
scrFI
mvali mnlI
ecorII
dsav
bstNI econI
apyI[dcn+] mnlI
bsaJI bslI ddeI
mnlI
901 GTGACAGGA TCATGCAGGA ATTGTGAAAGT GACACGTTTT TCCAGAGAAAT TGAATTTGGGG AAATATAAAC CTCTCCOAGA ATACCCAGGC GTCCTCTCTG
CACTGTTCCT AGTACGTCTT TAAACTTTCA CTGTGCAAAA AGGGTCITTA ACTAAACCCC TTTATATTG GAGAGGTCT TATGGGTCCG CAGGAGAGAC
nlaIII
sau3AI
mboI/ndeII[dam-]
dpmI[dam+]
dpmI[dam-]
maeIII
maeIII alwI[dam-] apoI
901 GTGACAGGA TCATGCAGGA ATTGTGAAAGT GACACGTTTT TCCAGAGAAAT TGAATTTGGGG AAATATAAAC CTCTCCOAGA ATACCCAGGC GTCCTCTCTG
CACTGTTCCT AGTACGTCTT TAAACTTTCA CTGTGCAAAA AGGGTCITTA ACTAAACCCC TTTATATTG GAGAGGTCT TATGGGTCCG CAGGAGAGAC
scrFI
mvali
ecorII
dsav
bstNI
apyI[dcn+]
sau96I
avaII
asuI mnlI sfaNI accI mboII mboII mnlI aluI
1001 AGGTCCAGGA GGAAGAGGC ATCAAGTATA AGTTTGAAGT CTACGAGAGG AAGACTAAC AGGAAGATGC TTTCAGATTC TCTGCTCCCC TCCTAAAGCT
TCCAGGTCTT CTTTTTCCG TAGTTCATAT TCAAACTTCA GATGCTCTTC TTTCTGATTG TCCTTCTACG AAAGTTCAAG AGACGAGGGG AGGATTTCGA
^END DHR
styI
bsaJI
sau3AI
mboI/ndeII[dam-]
dpmI[dam+]
dpmI[dam-]
alwI[dam-]
bstXI/xhoII
cac8I
ppl10I
nsII/avaIII
bsaJI
1101 ATGCATTTT ATAAGACCAT GGGACTTTT CTGGCTTTAG ATCCCTTTGG CTTCGTTAGA AGCAGCTAC AATAATACA TAACCTTATG TATCATACAC
TACGTAAAAA TATTCTGGTA CCCTGAAAA GACCGAAATC TAGGGGAACC GAAGCAATCT TGCCTCGATG TTAATTATGT ATTGGAATAC ATAGTATGTC
sau96I
avaII
asuI
scrFI
mvali
ecorII

```

FIG. 48D

1201 ATACGATTTA GGTGACACTA TAGATAACAT CCACCTTTGCC TTTCTCTCCA CAGGTGTCCA CTCCACAGGTC CAACCTGCACC TCGGTTCTAT CGATTGAATT
 TATGCTAAAT CCACCTGTGAT ATCTATTGTA GGTGAAACGG AAAGAGAGGT GTCCACAGGT GAGGTCCAG GTTGACCTCG AGCCAAGATA GCTAACTTAA
 seq from PRK6G425VH: Cla-AvrII^

maelIII hphi scfI foki
 dsav bstNI apyI[dcmt+] mnli bsaJI
 ecorI taqI apol
 claiI/bsp106
 bspDI[dam-]
 1201 ATACGATTTA GGTGACACTA TAGATAACAT CCACCTTTGCC TTTCTCTCCA CAGGTGTCCA CTCCACAGGTC CAACCTGCACC TCGGTTCTAT CGATTGAATT
 TATGCTAAAT CCACCTGTGAT ATCTATTGTA GGTGAAACGG AAAGAGAGGT GTCCACAGGT GAGGTCCAG GTTGACCTCG AGCCAAGATA GCTAACTTAA

scrFI mval fnu4HI
 ecorII dsav
 bstNI bsoFI
 apyI[dcmt+] haeI bbvI
 acII haeII/pali
 1301 CCACCATGGG ATGGTCATGT ATCATCCTTT TTCTAGTAGC AACTGCAACT GGAGTACATT CAGAAGTTCA GCTAGTGCAG TCTGGCGGTG GCCTGGTGCA
 GGTGGTACCC TACCAGTACA TAGTAGGAAA AAGATCATCG TTGACGTGA CCTCATGTAA GTCTCAAGT CGATCACGTC AGACCGCAC CGGACCACGT
 E V Q L V Q S G G L V Q

scrFI

ncII

mspi

hpaiI

dsav

caulI

xmaI/pspAI

smaI

scrFI

ncII

dsav

caulI

bsli

bsaJI

bsstNI

bsaJI

bsli

bsstNI

bsaJI

bsli

bsstNI

bsaJI

bsli

bsstNI

bsaJI

bsli

bsstNI

bsaJI

bsli

bsstNI

bsaJI

bsli

bsstNI

bsaJI

bsli

bsstNI

bsaJI

bsli

FIG. 48E

hgiJII
 bsp1286
 bmyI

scrFI

mval banII

ecorII

dsav

bstNI

bsaJI

apyI[dcmt+]

gccagggggc

tcactccggt

tgctcgtgac

acaggacacg

tcgaagacgg

atgaggaagg

atgaggaagg

atgaggaagg

atgaggaagg

atgaggaagg

atgaggaagg

atgaggaagg

atgaggaagg

atgaggaagg

1401 GCCAGGGGCG TCACCTCCGTT TGTCCTGTGC AGCTTCTGGC TACTCCTTCT CGATCCTACTA TATGCACCTGG GTCCGTGAGG CCCCCTGGTAA GGGCCTGGAA

CGGTCCCGCG AGTGAGGCAA ACAGGACACG TCGAAGACGG ATGAGGAAGG GTCAAGTAT ATAGTGACC CAGGCAGTCC GGGGCCCAT CCCGGACCTT

14 P G G S L R L S C A A S G Y S F S S H Y M H W V R Q A P G K G L E

[illegible]

FIG. 48F

1801 CTGGCTGCC TGGTCAAGGA CTACTTCCC GAACCGGTGA CGGTGTCGTG GAATCAGGC GGCCTGACCA CGCGGTGCA CACCTTCCC GCTGTCTTAC
 1802 GACCGACGG ACCAGTTCCT GATGAAGGG CTTGGCCACT GCCACAGCAC CTTGAGTCCG CGGACTGCT GTGGAGGCG CGACAGGATG
 1803 L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q

scrFI hgiAI/aspHI hinPI
 mvaI nlaIV nari bsp1286
 ecoRII kasI hinII/acyI mspI
 ecoNI hgiCI cac8I hpaII
 deaV haeII fnu4HI scrFI
 bstNI bsaI ahaII/bsaHI acilI apaLI/snoI deaV
 belI cfr10I/bsrFI bsaI
 apyI[dcM+] fnu4HI ageI tth111I/aspI ddeI hhaI/cfoI nspBII alw41I/snoI caulI scfI
 bsoFI bsaI bslI
 bbVI bslI CTGGCTGCC TGGTCAAGGA CTACTTCCC GAACCGGTGA CGGTGTCGTG GAATCAGGC GGCCTGACCA CGCGGTGCA CACCTTCCC GCTGTCTTAC
 1801 GACCGACGG ACCAGTTCCT GATGAAGGG CTTGGCCACT GCCACAGCAC CTTGAGTCCG CGGACTGCT GTGGAGGCG CGACAGGATG
 147 L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q

fnu4HI nlaIV
 bsoFI hgiCI
 rnaI bsaI
 bsp1286 maeI
 maeIII bfaI aluI bsp1286
 hphi bmyI mnlI bbVI bmyI
 fnu4HI fnu4HI
 bsoFI bsoFI
 mnlI bbVI
 eco8II mnlI bsoFI
 bsa36I/matII/sauI ddeI
 hphi bmyI mnlI bbVI bmyI
 1901 AGTCCTCAGG ACTCTACTCC CTCAGCAGCG TGGTACTGT GCCCTCTAGC AGCTTGGGCA CCCAGACCTA CATCTGCAAC GTGAATCACA AGCCCAGCAA
 TCAGGAGTCC TGAGATGAGG GAGTCGTCC ACCACTGACA CGGGAGATCG TCGAACCCGT GGGTCTGGAT GTAGACGTTG CACTTAGTGT TCGGGTCGTT
 181 S S G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N

ahdI/eam1105I
 sau96I
 avall
 scrFI
 mvaI asuI
 ecoRII
 deaV
 bstNI nlaIV mboII
 bsaI bsmFI bpuAI
 bmyI alwNI[dcM-] apyI[dcM+] bbsI mnlI
 2001 CACCAAGGTG GACAAGAAAG TTGAGCCCAA ATCTTGTGAC AAAACTCACA CATGCCACC GTGCCAGCA CCTGAACCTC TGGGGGACC GTCAGTCTTC
 GTGTTCCAC CTGTTCTTTC AACTCGGGTT TAGAACACTG TTTTGAGTGT GTAGCGGTG CACGGGTGCG GACTTGAGG ACCCCCTGG CAGTCAGAAG
 214 T K V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F

FIG. 48G

sau96I
nlaIV
mspI
hpaII
scrFI
ncII
dsav
sau3AI auaII nlaIII
mboI/ndeII[dam-] nspl
nlaIII cauII mnli nspHI
rcal dplI[dam+] ddel mslI
mnli dplII[dam-] eco8II maelII
styl mslI bspHI[dam-] asuI bsu36I/mstII/sauI
mboII earI/ksp632I bsaJI
2101 CTCTTCCCC CAAACCCCA GGACACCCCTC ATGATCTCC GGACCCCTGA GGTCACATGC GTGGTGGTGG ACGTGAGCCA CGAGAGACCCT GAGGTCAAGT
GAGAAGGGG GTTTGGGT CCTGTGGAG TACTAGAGG CCTGGGGACT CCAGTGTACG CACCACCACC TGCACCTGGT GCTTCTGGGA CTCCAGTCA
247 L F P P K P K D T L M I S R T P E V T C V V V D V S H E D P E V K F

acil
thai
fnuDI/mvnl
bstUI
bsh1236I
sacII/stII
nspBII
kspI
dsaI
bsaJI
acil
fnu4HI mnli rsal
bsaJI bseRI csp6I
bsaFI bseRI csp6I
2201 TCAACTGGTA CGTGGACGGC GTGGAGGTGC ATAATGCCAA GACAAAGCCG CGGGAGGAGC AGTACAACAG CACGTACCGT GTGGTCAGCG TCCTCACCGT
AGTTGACCAT GCACCTGCCG CACCTCCAG TATTACGGTT CTGTTTCGGC GCCCTCCTCG TCATGTTGTC GTGCATGGCA CACCAGTCGC AGGAGTGGCA
281 N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V

maelII
rsal
csp6I
bsrI bsaAI
scrFI
mval
ecorII
dsav
econoI batNI bsrI
bslI apyI[dam+]
2301 CCTGCACCAG GACTGGCTGA ATGGCAAGGA GTACAAAGTGC AAGGTCTCCA ACAAGCCCT CCCAGCCCCC ATCGAGAAAA CCATCTCCAA AGCCAAAGGG
GGACGTGGTC CTGACCGACT TACCGTTCCT CATGTTACG TTCCAGAGGT TGTTTCGGGA GGGTGGGGG TAGCTCTTTT GGTAGAGGTT TCGGTTTCCC
314 L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G

fnu4HI bsoFI
bsaFI
bbvI
2301 CCTGCACCAG GACTGGCTGA ATGGCAAGGA GTACAAAGTGC AAGGTCTCCA ACAAGCCCT CCCAGCCCCC ATCGAGAAAA CCATCTCCAA AGCCAAAGGG
GGACGTGGTC CTGACCGACT TACCGTTCCT CATGTTACG TTCCAGAGGT TGTTTCGGGA GGGTGGGGG TAGCTCTTTT GGTAGAGGTT TCGGTTTCCC
314 L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G

FIG. 48H

[illegible]

FIG. 48I

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```

scrFI      sau96I      acII      haeIII/palI
ncII      fnu4HI      asuI
mspI      bsoFI      nlaIII
hpaII      sfiI      styI      aluI
dsav      eaeI      ncoI      fnu4HI
bsmAI      sau96I      hinFI      pstI      dsal      bsoFI
baII      haeIII/palI      bsgI      aluI      haeII/palI      bbvI      maeIII
cauII      asuI      bfaI      accI      bspMI      hindIII      bgII      bsaJI      TGCAGCTTAT      AATGGTTACA
2701 TCCCTGTCTC      GGGGTAAATG      AGTGGGACCG      CCTAGAGTC      GACCTGCAGA      AGCTTGGCCG      CCATGGCCCA      ACTTGTATTAT      TGAACAAATA      ACCTCGAATA      TTACCAATGT
AGGGACAGAG      GCCCATTTAC      TCACGCTGCC      GGGATCTCAG      CTGGACGTCT      TCGAACCGCG      GGTACCGGGT      TGAACAAATA      ACCTCGAATA      TTACCAATGT
447 S L S P G K O

sfaNI      apoI      rmaI
tagI      pleI      rmaI      salI      scfI      maeI      hincII/hindII      eaeI      ncoI      fnu4HI      asuI      bsoFI      nlaIII
2801 AATAAGCAA      TAGCATCACA      AATTTCACAA      ATAAAGCATT      TTTTTCACGTG      CATCTAGTT      GTGGTTGTC      CAAACTCATC      AATGTATCTT      ATCATGTCTG
TTATTTCGTT      ATCGTAGTGT      TTTAAAGTGT      TATTTCGTAA      AAAAAGTGAC      GTAAGATCAA      CACCAACACAG      GTTGAGTAG      TTACATAGAA      TAGTACAGAC
nlaIII      alwI[dam-]

sau3AI      mboI/ndeII[dam-]
dpnI[dam+]
dpnII[dam-]
pvuI/bspCI
mcrI
bsiEI
taqI[dam-]      tru9I
clai/bsp106[dam-]
bspDI[dam-]      mseI
sau3AI      xmnI
mboI/ndeII[dam-]      hinPI      dsal      haeIII/palI
dpnI[dam+]      asp700      hhaI/cfoI      nlaIII
dpnII[dam-]      aseI/asnI/vspI      bsaJI
2901 GATCGATCGG      GAATTAATTC      GCGCAGCAC      CATGGCCTGA      AATAACCTCT      GAAAGAGGAA      CTTGGTTAGG      TACCTTCTGA      GCGGGAAGA      ACCATCTGTG
CTAGTAGCC      CTTAATTAAAG      CCGCGTCGTG      GTACCGGACT      TTATTGGAGA      CTTTCTCCTT      GAACCAATCC      ATGGAAGACT      CCGCCTTCTT      TGGTAGACAC

```

FIG. 48J

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```

scrFI      sfaNI      ppulOI      scrFI
mvaI      nsII/avaIII  mvaI      mvaI
ecoRII    nlaIII      ecorII    ecorII
dsav      sphi      dsav      dsav
bstNI     nspi      bstNI     bstNI
apyI[dcM+]  bsajI    nspHI    apyI[dcM+]
                        cac8I      sexAI      bsmFI
                        bsmFI    nlaIV      cac8I
                        GTGAAAGTC CCCAGGCTCC CCAGCAGGCA GAAGTATGCA AAGCATGCAT CTCAAATTAGT CAGCAACCAG GTGTGGAAAG
3001 GAATGTGTGT CAGTTAGGGT GTGAAAGTC CCCAGGCTCC CCAGCAGGCA GAAGTATGCA AAGCATGCAT CTCAAATTAGT CAGCAACCAG GTGTGGAAAG
CTTACACACA GTCAATCCCA CACCTTTTCAG GGTGCGGAGG GGTGCTCGGT CTTTCATACGT TTCGTACGTA GAGTTAATCA GTCGTTGGTC CACACCTTTC

                        sfaNI
                        ppulOI      nsII/avaIII
                        nlaIII
                        sphi      nspi      nspHI      cac8I
                        bstNI     nspI      nspHI      cac8I
                        apyI[dcM+]  bsajI    nspHI      cac8I
                        bsmFI    nlaIV      cac8I
                        GTGAAAGTC CCCAGGCTCC CCAGCAGGCA GAAGTATGCA AAGCATGCAT CTCAAATTAGT CAGCAACCAG GTGTGGAAAG
3101 TCCCAGGCT CCGCAGCAGG CAGNAGTATG CAAGCATGCG ATCTCAATTA GTCAGCAACC ATAGTCCGCG CCCTAACCTCC GCCCATCCCG CCCCTAACTC
AGGGGTCCGA GGGGTGCTCC GTCTTCATAC GTTTCGTACG TAGAGTTAAT CAGTCTGTTGG TATCAGGGCG GGGATTGAGG CGGTAGGGC GGGGATTGAG

                        nlaIII
                        styI      ncoI
                        bsII dsai
                        acII bsajI
                        bsrI acII
                        CGCCAGTTC CGCCCATTCCT CCGCCCATTC CCGCCCATTC TATGCTGATG TATGCTGATG TATGCTGATG TATGCTGATG TATGCTGATG
3201 CGCCAGTTC CGCCCATTCCT CCGCCCATTC CCGCCCATTC TATGCTGATG TATGCTGATG TATGCTGATG TATGCTGATG TATGCTGATG
GGGGTCAAG GGGGGTAAGA GCGGGGGTAC CGACTGATTA AAAAAAATAA ATACGCTCTCC GGTCCGGCG GAGCGGGAGA CTCGATAAGG TCTTCATCAC

```

FIG. 48K

```

scrFI
ncII
mspI
hpaII
dsav
haeIII/palI
mcrl
eagI/xmaIII/eclXI
eaeI
cfrI
bsiEI
mspI caulI
hpaII
alul
rmaI
maeI
bfaI
nheI
cac8I
alul
mnII bfaI
mnII
3301 AGGAGGCTTT TTTGGAGGCC TAGGCTTTTG CAAAAGCTA GCTTATCCG CGGGGAACGG TGCATTGGAA CGCGGATTCC CCGTGCCTAG AGTCAGGTAA
TCCTCGAAA AAACCTCCGG ATCCGAAAC GTTTTTCGAT CGAATAGGCC GGCCTTGCC AGTAACTT GCGCCTAAGG GGCACGGTTC TCAGTCCATT
^seq from pSV16B5-6G4VL: AvrII - HindIII frag
U1 matched splice donar^

sau3AI
mboI/ndeII[dam-]
dpnI[dam+]
dpuII[dam-]
alwI[dam-]
taqI[dam-]
clai/bsp106[dam-]
bspDI[dam-]
sau3AI
mboI/ndeII[dam-]
dpnI[dam+]
dpuII[dam-]
alwI[dam-]
fnu4HI
bscFI
acII
thai
fnuDI/mvnI tru9I
bstUI
msei
bsh1236I aseI/asnI/vspI
bsh1236I
3401 GTACCGCTA TAGAGTCTAT AGGCCACCC CCTTGCTTC GTTAGAACGC GCCTACATTT AATACATAAC CTTTGGATC GATCCTACTG ACACGTGACAT
CATGGCGGAT ATCTCAGATA TCCGGGTGGG GGAACCGAAG CAATCTGCG CCGATGTTAA TTATGTATTG GAAAACCTAG CTAGGATGAC TGTGACTGTA
^sp6 promoter
^removed ATG
^U2 match
lariat consensus^
IqG vH natural lariat restored^

```

FIG. 48L

```

sau96I
avaII
asuI
scrFI
mvaI
ecoRII
dsav
bstNI
apyI[dcam+]
belI bsaJI
3501 CCACTTTTTC TTTTCTCCA CAGGTGTCCA CTCCTCAGGTC CAACTGCACC TCGGTTCGGG AAGCTAGCTT GGGCTGCATC GATTGAATTC CACCATGGGA
GGTGA AAAAGAGGT GTCCACAGGT GAGGGTCCAG GTTGACGTGG AGCAAGCGC TTGCATCGAA CCCGACGTAG CTTAACTTAAG GTGGTACCCT
^cloning linker

3601 TGGTCATGTA TCATCCTTTT TCTAGTAGCA ACTGCAACTG GAGTACATTC AGATATCCAG ATGACCCAGT CCGCGAGCTC CCTGTCCGCC TCTGTGGGCG
ACCAGTACAT AGTAGGAAA AGATCATCGT TGACGTTGAC CTCATGTAAG TCTATAGGTC TACTGGGTCA GGGGCTCGAG GGACAGGCGG AGACACCGCG
D I Q M T Q S P S S L S A S V G D
1

3701 ATAGGTCAC CATCACTGC AGGTCAAGTC AAAGCTTAGT ATCATGGTATA GGTGCTACGT ATTACTACTG GTATCAACAG AAACACAGAA AAGCTCCGAA
TATCCAGTG GTAGTGACG TCCAGTTCAG TTTCGAATCA TGTACCATAT CCACGATGCA TAAATGTGAC CATAGTTGTC TTTGGTCTT TTCGAGGCTT
18 R V T I T C R S S Q S L V H G I G A T Y L H W Y Q Q K P G K A P K

```

FIG. 48M

3801 ACTACTGATT TACAAAGTAT CCAATCGATT CTCTGGAGTC CCTTCTCGCT TCTCTGGATC CGGTCTGGG ACGGATTTC A CTCTGACCAT CAGCAGTCTG
 TGATGACTAA ATGTTTCATA GGTTAGCTAA GAGACCTCAG GGAAGACCGA AGAGACCTAG GCCAAGACCC TGCCTAAGT GAGACTGGTA GTCGTCAGAC
 51 L L I Y K V S N R F S G V P S R F S G S G T D F T L T I S S L

mspI
 hpaII
 bslI
 bsaWI
 sau3AI
 mboI/ndeII[dam-]
 dpnI[dam+]
 dpnII[dam-]
 alwI[dam-]
 nlaIV
 bstYI/xhoII
 bamHI
 alwI[dam-] bsmFI
 fnu4HI
 bsoFI
 bbvI
 scfI
 pstI
 bsgI

rsaI
 csp6I
 nlaIV
 kpnI styI
 hgiCI
 banI bsaJI
 asp718
 acc65I
 sau3AI
 mboI/ndeII[dam-] fnu4HI
 dpnI[dam+]
 dpnII[dam-]
 gatCAACGA ACTGTGGCTG
 CCAAGGTGGA GGACAGGGTA CCTGTCCCAT GGTTCACCT CTAGTTGCT TGACACCCGAC
 84 Q P E D F A T Y Y C S Q S T H V P L T F G Q G T K V E I K R T V A A

mboII
 bpuAI
 bbsI
 mboII aciI
 asp700
 csp6I
 scaI
 nlaIII
 maeII
 bsrBI
 aciI
 bsmFI
 xmnI
 asp700
 cac8I
 asp700
 haeII/palI
 haeI
 mnlI

FIG. 48N

[illegible]

FIG. 480

[illegible]

FIG. 48P

4701 ATCTCAATTA GTCAGCAACC ATAGTCCGCG CCTPAACTCC GCCCATCCCG CCCTAACTC CGCCAGTTC CGCCATTCT CGCCCATG GCTGACTAAT
 TAGAGTTAAT CAGTCGTGG TATCAGGCGG GGGATTGAG GGGTAGGGC GGGGTCAAG CGGGTAAGA GCGGGGTAC CGACTGATTA

acilI fnu4HI
 bsmFI acilI foki acilI bsaJI
 4701 ATCTCAATTA GTCAGCAACC ATAGTCCGCG CCTPAACTCC GCCCATCCCG CCCTAACTC CGCCAGTTC CGCCATTCT CGCCCATG GCTGACTAAT
 TAGAGTTAAT CAGTCGTGG TATCAGGCGG GGGATTGAG GGGTAGGGC GGGGTCAAG CGGGTAAGA GCGGGGTAC CGACTGATTA

rmaI
 maeI
 styI
 bsaJI
 blnI
 avrII[dam-]
 haeIII/palI
 stuI
 haeI
 mnlI bfaI
 maeIII
 aluI
 4801 TTTTCTTATT TATGAGAGG CCGAGCGCG CTGGCCTCT GAGCTATTCC AGAAGTAGTG AGGAGGCTTT TTTGGAGGC TAGGCTTTTG CAAAAGCTG
 AAAAAAATAA ATACGTCTCC GGCTCCGCG GAGCGGAGA CTCGATAAGG TCTTCATCAC TCCTCCGAAA AACCTCCGG ATCCGAAAC GTTTTTCGAC
 start pUC118^

fnu4HI
 haeIII/palI
 mcrI
 eagI/xmaIII/eclXI
 eaeI
 notI
 barBI bsoFI
 taqI cfrI
 xhoI fnu4HI
 paeR7I bslEI
 avai bsoFI
 mnlI acilI acilI
 4901 TTACTCTGAG CGCGCGCTTA ATTAAGGCGC GCATTTTAA TCCTGCAGGT AACAGCTTGG CACTGGCGGT CGTTTACAA CGTCGTGACT GGGAAACCC
 AATGAGCTC GCGGCGAAT TAATTCCGCG CGGTAAATTT AGGACCTCCA TTGTCAACC GTGACCGGCA GCAAAATGTT CGAGCACTGA CCCTTTTGGG
 ^linearization linker inserted into HpaI site

FIG. 48Q

[illegible]

FIG. 48B

mspI
 hpaII
 naeI
 cfr10I/bsrFI
 maeII cac8I
 5301 TTTCTCGCCA CGTTCGCCGG CTTTCCCGGT CAGCTCTAA ATCGGGGGCT CCCTTAGG TCCGATTTA GTGCTTTACG GCACCTCGAC CCCAAAAAAC
 AAAGACGGT GCAAGCGGCC GAAAGGGCA GTTCGAGATT TAGCCCCCGA GGGAATCC AAGCTAAAT CACGAAATGC CGTGAGCTG GGGTTTTTGTG
 nlaIV
 hgiJII
 bsp1286
 bmyI
 banII
 aluI
 maeII haeIII/palI
 draIII sau96I
 bsaAI asuI
 hphI
 5401 TTGATTGGG TGATGGTTCA CGTAGTGGC CATGCCCTG ATAGACGGT TTTGCCCCIT TGACCTTGA GTCCACGTC TTTAATAGTG GACTCTTGT
 AACTAAACCC ACTACCAAGT GCATCACCG GTACGGGAC TATCTGCCA TATCTGCCA AAGCGGGA ACTGCAACCT CAGGTGCAAG AATTATCAC CTGAGAACAA
 maeII pleI
 drdI hinfI maeII mseI
 5401 TTGATTGGG TGATGGTTCA CGTAGTGGC CATGCCCTG ATAGACGGT TTTGCCCCIT TGACCTTGA GTCCACGTC TTTAATAGTG GACTCTTGT
 AACTAAACCC ACTACCAAGT GCATCACCG GTACGGGAC TATCTGCCA TATCTGCCA AAGCGGGA ACTGCAACCT CAGGTGCAAG AATTATCAC CTGAGAACAA
 tru9I
 mseI
 haeIII/palI
 5501 CCAAACTGGA ACAACACTCA ACCCTATCTC GGGCTATTCT TTTGATTAT AAGGATTTT GCGGATTTCG GCTATTGTG TAAAAATGA GCTGATTAA
 GGTTCACCT TGTGTGAGT TGGGATAGAG CCCGATAAGA AAACCTAATA TTTCCCTAAA CGGCTAAAGC CGGATAACCA ATTTTACT CCACTAAAT
 hgiAI/aspHI
 bsp1286
 bsiHKAI
 bmyI ddeI
 apaII/snoI rsaI
 alw44I/snoI csp6I
 5601 CAAAAATTTA ACGCGAATT TTAACAAATA TTAACGTTTA CAATTTTATG GTGCACTCTC AGTACAATCT GCTCTGATGC CGCATAGTGA AGCCTACTCC
 GTTTTAAAT TCGCTTAAA ATTGTTTAT AATTGCAAT GTTAAATAC CACGTGAGAG TCATGTAGA CGAGACTACG GCGTATCAAT TCGGTTGAGG
 thi
 fnuDII/mvnI
 maeII
 5601 CAAAAATTTA ACGCGAATT TTAACAAATA TTAACGTTTA CAATTTTATG GTGCACTCTC AGTACAATCT GCTCTGATGC CGCATAGTGA AGCCTACTCC
 GTTTTAAAT TCGCTTAAA ATTGTTTAT AATTGCAAT GTTAAATAC CACGTGAGAG TCATGTAGA CGAGACTACG GCGTATCAAT TCGGTTGAGG
 apoI bsh1236I
 5601 CAAAAATTTA ACGCGAATT TTAACAAATA TTAACGTTTA CAATTTTATG GTGCACTCTC AGTACAATCT GCTCTGATGC CGCATAGTGA AGCCTACTCC
 GTTTTAAAT TCGCTTAAA ATTGTTTAT AATTGCAAT GTTAAATAC CACGTGAGAG TCATGTAGA CGAGACTACG GCGTATCAAT TCGGTTGAGG
 hinPI
 hhaI/cfoI
 fnu4HI
 bsoFI
 maeIII
 5601 CAAAAATTTA ACGCGAATT TTAACAAATA TTAACGTTTA CAATTTTATG GTGCACTCTC AGTACAATCT GCTCTGATGC CGCATAGTGA AGCCTACTCC
 GTTTTAAAT TCGCTTAAA ATTGTTTAT AATTGCAAT GTTAAATAC CACGTGAGAG TCATGTAGA CGAGACTACG GCGTATCAAT TCGGTTGAGG
 mspI
 hpaII
 scrFI
 nciI
 dsav foki
 cauII aciI
 5701 GCTATCGCTA CGTGAATGGG TCATGGCTGC GCCCGACAC CGCGTACGC GCCCTGACGG GCTGTCTGC TCCCGGATC CGCTACAGA
 CGATAGCGAT GCACTGACCC AGTACCGAG CGGGCTGTG GCGGCTGTG GCGGCTGTG GCGGCTGTG GCGGCTGTG GCGGCTGTG GCGGCTGTG

FIG. 48S

[illegible]

FIG. 48T

[illegible]

FIG. 48U

hinPI mspI
 hhaI/cfoI hpaII
 mstI aluI scrFI
 aviII/fspI bsrI rmaI nciI tru9I
 maeII tru9I msel
 psp1406I bfaI caulI aseI/asnI/vspI
 6601 CGACGAGCGT GACACCAGCA TGCCAGCAGC AATGGCAACA AACTATTAAAC TGGCGAACTA CTTACTCTAG CTTCOCGGCA ACAATTAATA
 GCTGCTCGCA CTGTGGTGCT ACGGTGCTCG TTACCGTTGT TGCACGCGT TTGATAATTG ACCGCTTGAT GAATGAGATC GAAGGCCGT TGTAAATTAT
 bglI mspI
 sau96I cac8I hpaII
 haeIII/palI cfr10I/bsrFI
 hinPI asuI mspI nlaIV hphI bsmAI
 hhaI/cfoI hpaII bpmI/gsuI[dcm-] bsaI
 6701 GACTGGATGG AGCGGATAA AGTTGCAGGA CCACTTCTGC GCTCGGCCCT TCCGGCTGCC TGGTATTATG CTGATAAATC TGGAGCCGGT GAGCGTGGT
 CTGACCTACC TCCGCTATT TCAACGTCCT GGTGAAGACG CGAGCCGGGA AGCCCGACCG ACCAATAAAC GACTATTATG ACCTCGGCCA CTCGCACCCA
 aciI
 thaI fnu4HI haeIII/palI pleI
 fnuDII/mvnI bsoFI sau96I hinfi
 bstUI nlaIV ahdI/eam1105I fokI
 bsh1236I bsrDI bsrI asuI mnli
 6801 CTGCGGTAT CATTCAGCA CTGGGGCAG ATGGTAAGCC CTCCGCTATC GTAGTTATCT ACACGACGGG GAGTCAGGCA ACTATGGATG AACGAATAG
 GAGGCCATA GTAACGTCGT GACCCCGGTC TACCATTCCG GAGGGCATAG CATCAATAGA TGTGCTGCC CTCAGTCCGT TGATACCTAC TTGCTTTATC
 ddeI
 sau3AI nlaIV tru9I
 mboI/ndeII[dam-] msel
 dpnI[dam+] hgiCI ahaII/draI msel tru9I
 dpnII[dam-] bni mnli maeIII
 6901 ACAGATCGCT GAGATAGGTG CCTCACTGAT TAAGCATTGG TAACCTGTCAG ACCAAGTTTA CTCATATATA CTTTAGATTG ATTTAAACT TCATTTTAA
 TGTCTAGCGA CTCTATCCAC GGAGTGACTA ATTGCTAACC ATTGACAGTC TGGTTCAAT GAGTATATAT GAAATCTAAC TAAATTTTGA AGTAAAAAT
 rmaI sau3AI
 maeI sau3AI mboI/ndeII[dam-]
 sau3AI hphI mboI/ndeII[dam-]
 mboI/ndeII[dam-] dpnI[dam+] dpnI[dam+] hgaI
 dpnII[dam-] dpnII[dam-] dpnII[dam-] ddeI
 tru9I bstVI/xhoII alwI[dam-] nlaIII maeII
 msel alwI[dam-] bstVI/xhoII rcaI tru9I
 ahaII/draI bfaI mboII[dam-] msel
 7001 TTTTAAAGGA TCTAGTGAA GATCCTTTT GATAATCTCA TGACCAAAAT CCTTAACT GAGTTTTCGT TCCACTGAGC GTCAGACCCC GTAGAAAAA
 AAATTTTCT AGATCCACTT CTAGGAAAAA CTATTAGAGT ACTGTTTGA GGAATTGCA CTCAAAAACA AGGTGACTCG CAGTCTGGG CATCTTTCT

FIG. 48V

FIG. 48W

```

sau3AI
mboII[dam-]
sau3AI mboI/ndeII[dam-] thai
mboI/ndeII[dam-] fnuDII/mvni
dnpI[dam+] dnpI[dam+] bstUI cac8I
dnpII[dam-] dnpII[dam-] bshI236I fnu4HI
bstYI/xhoII alwI[dam-] hinPI bsoFI
alwI[dam-] bstYI/xhoII hhai/cfoI bbvI
7101 TCAAAGGATC TTCTTGAGAT CCTTTTTC TGCGCGTAAT CTGCTGCTTG CAAACAAAAA AACCAACGCT ACCAGCGGTG GTTTGTTTGC CGGATCAAGA
AGTTTCTCTAG AAGAACTCTA GGAAGAAAAG ACGCGCATTA GAGACGAAC GTTTGTTTTT TTGGTGGGGA TGGTCGCCAC CAAACAACG GCCTAGTTCT
sau3AI
mboII[dam-]
sau3AI mboI/ndeII[dam-]
dnpI[dam+] dnpI[dam+] bstUI
dnpII[dam-] dnpII[dam-] bshI236I
bstYI/xhoII alwI[dam-] hinPI
alwI[dam-] bstYI/xhoII hhai/cfoI
7201 GCTACCAACT CTTTTCGGA AGGTAACCTGG CTTTCAGCAGA GCGCAGATAC CAAATACTGT CCTTCTAGTG TAGCGGTAGT TAGGCCACCA CTTCAAGAAC
CGATGGTTGA GAAAAAGGCT TCCATTGACC GAATGCTCT CCGCTCTATG GTTTATGACA GGAAGATCAC ATCCGGTGTG GAAGTTCTTG
sau3AI
mboII[dam-]
sau3AI mboI/ndeII[dam-]
dnpI[dam+] dnpI[dam+] bstUI
dnpII[dam-] dnpII[dam-] bshI236I
bstYI/xhoII alwI[dam-] hinPI
alwI[dam-] bstYI/xhoII hhai/cfoI
7301 TCTGTAGCAC CGGCTACATA CCTCGCTCTG CTAATCTGT TACCAGTGGC TGCTGCCAGT GCGGATAACT CGTGTCTTAC CGGGTTGGAC TCAAGACGAT
AGACATGGTG GCGGATGTAT GGAGCGAGAC GATTAGGACA ATGCTCACCG ACGACGCTCA CGCTATTCA GCACAGAATG GCCAACCTG AGTTCTGCTA
sau3AI
mboII[dam-]
sau3AI mboI/ndeII[dam-]
dnpI[dam+] dnpI[dam+] bstUI
dnpII[dam-] dnpII[dam-] bshI236I
bstYI/xhoII alwI[dam-] hinPI
alwI[dam-] bstYI/xhoII hhai/cfoI
7401 AGTTACCGGA TAAGCGCAG CGGTGGGGT GAACGGGGGG TTGCTGCACA CAGCCAGCT TGGAGCGAAC GACCTACACC GAACTGAGAT ACCTACAGCG
TCAATGGCCT ATTCCGGCTC GCCAGCCCGA CTTGCCCCCC AAGCACGTGT GTCGGGTGGA ACCTCGCTTG CTGGATGTGG CTTGACTCTA TGGATGTGCG
```

FIG. 48W

[illegible]

FIG. 48X

[illegible]

FIG. 48Y


```

tru9I
mseI
aseI/asnI/vspI
xmnl
nlaII    asp700
8101 TGACCATGAT TACGAATTAA
    ACTGGTACTA ATGCTTAATT
>length: 8120

aatII(GACGTC): 1690 5947
acc65I(GGTACC): 2969 3967 4529
accI(GTWMKAC): 823 1039 2738 4237
acII(CCGC): 217 229 238 250 260 271 317 422 454 485 574 1385 1795 1871 2248 2250 2758 2982
3167 3179 3188 3200 3210 3221 3267 3372 3404 3449 3686 3949 4021 4318 4542 4727
4739 4748 4760 4770 4781 4827 4910 4914 5070 5127 5153 5166 5203 5217 5220 5248
5275 5680 5699 5741 5751 5790 5979 6026 6125 6234 6311 6355 6476 6522 6713 6804
7166 7175 7310 7420 7541 7560 7687 7715 7806 7827 7834 7877 7901 7911 7967 8070
acyI
see hinII
aflII/bfrI(CTTAAG): 786
aflIII(ACRYGT): 932 7758
ageI(ACCGGT): 1833
ahaII/baHI(GRCGYC): 988 1690 1858 5117 5947 6329
ahaIII/draI(TTTAAA): 696 4935 6290 6982 7001
ahdI/eam1105I(GACNNNNNGTC): 2087 6865
    5 44 332 386 390 753 1097 1165 1370 1431 1951 2603 2751 2784 3282 3336 3340
aluI(AGCT): 3562 3566 3676 3733 3792 4270 4288 4311 4344 4554 4842 4896 4954 5047 5333 5590
5803 5822 6516 6579 6679 7200 7457 7593 7819 7937 8096
alw44I/snoI(GTGCAC): 1876 5651 6198 7444

```

FIG. 48Z

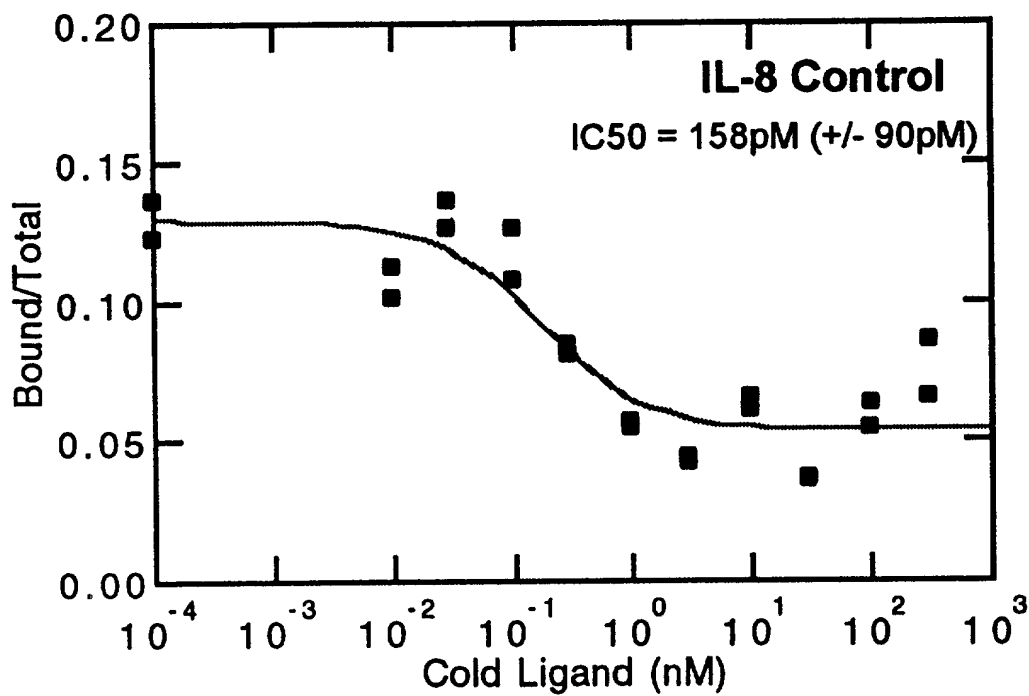


FIG. 49A

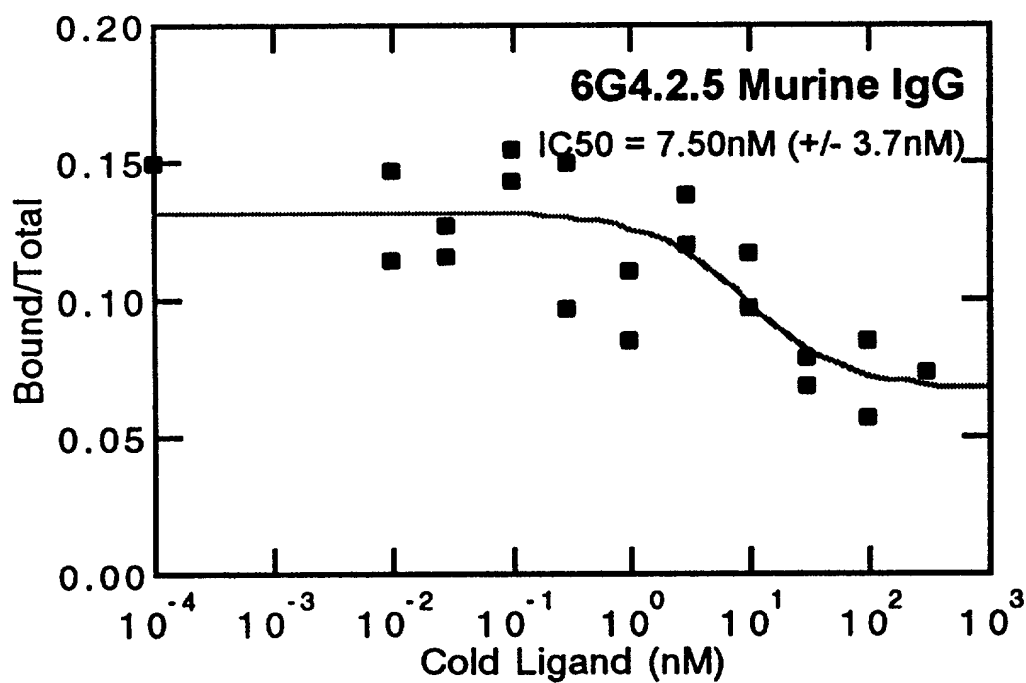


FIG. 49B

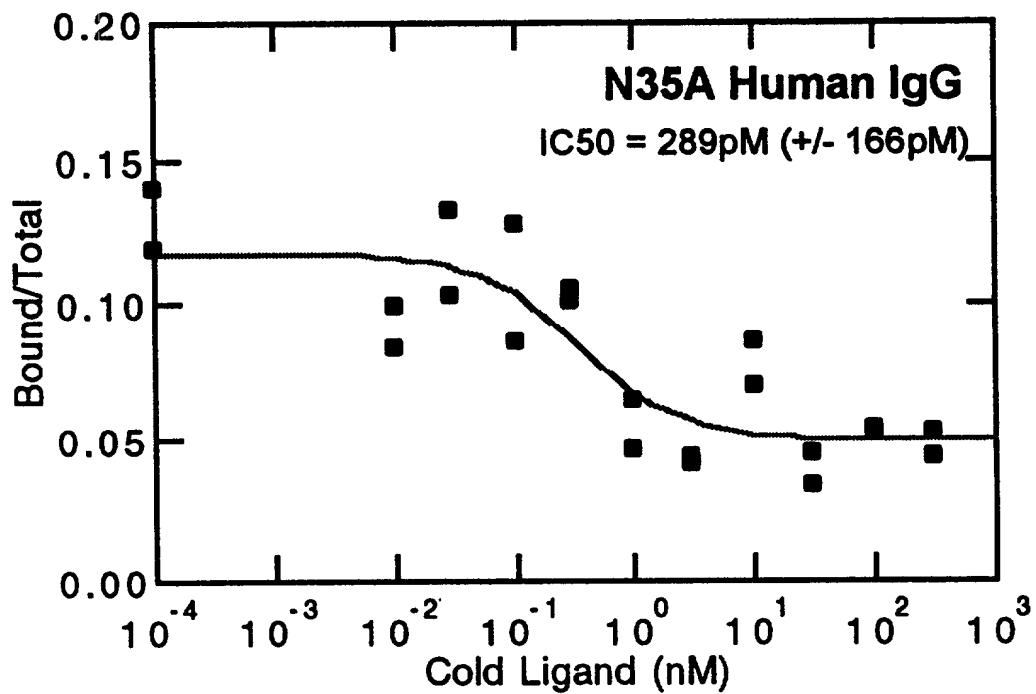


FIG. 49C

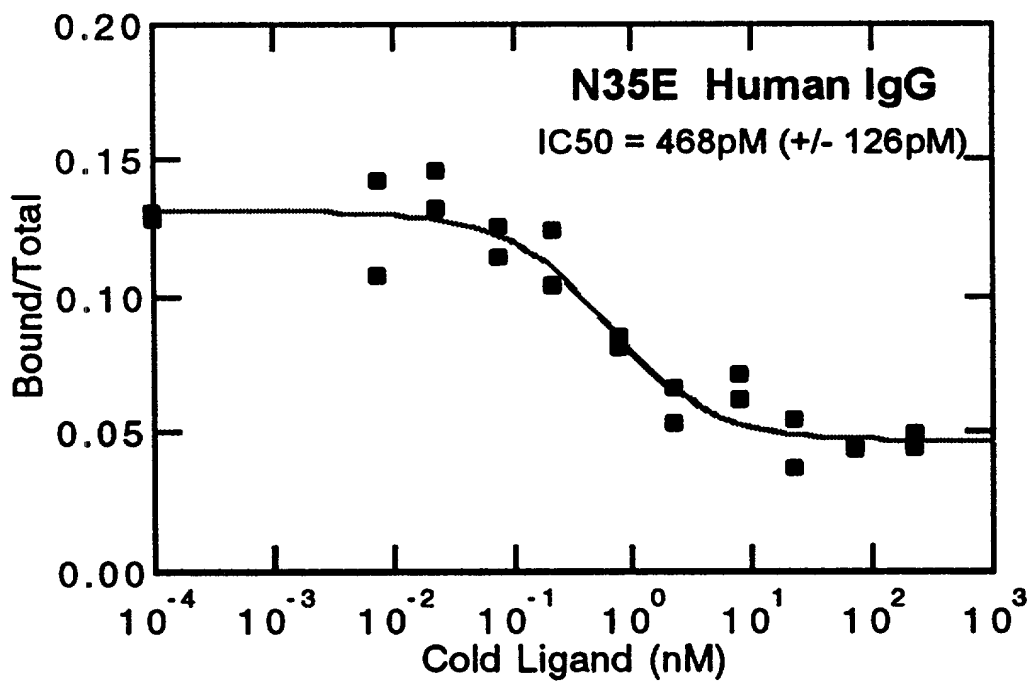


FIG. 49D

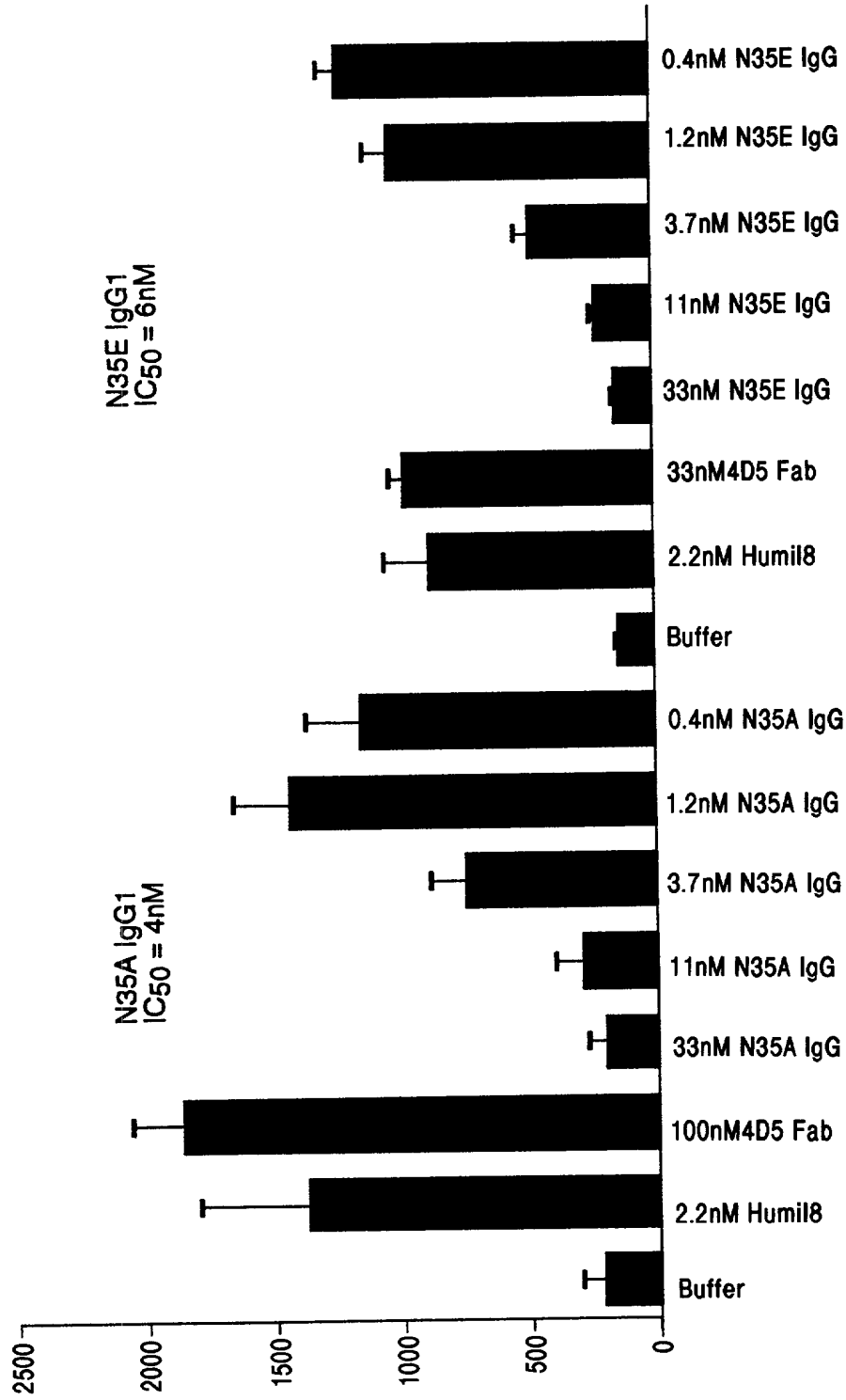


FIG. 50A

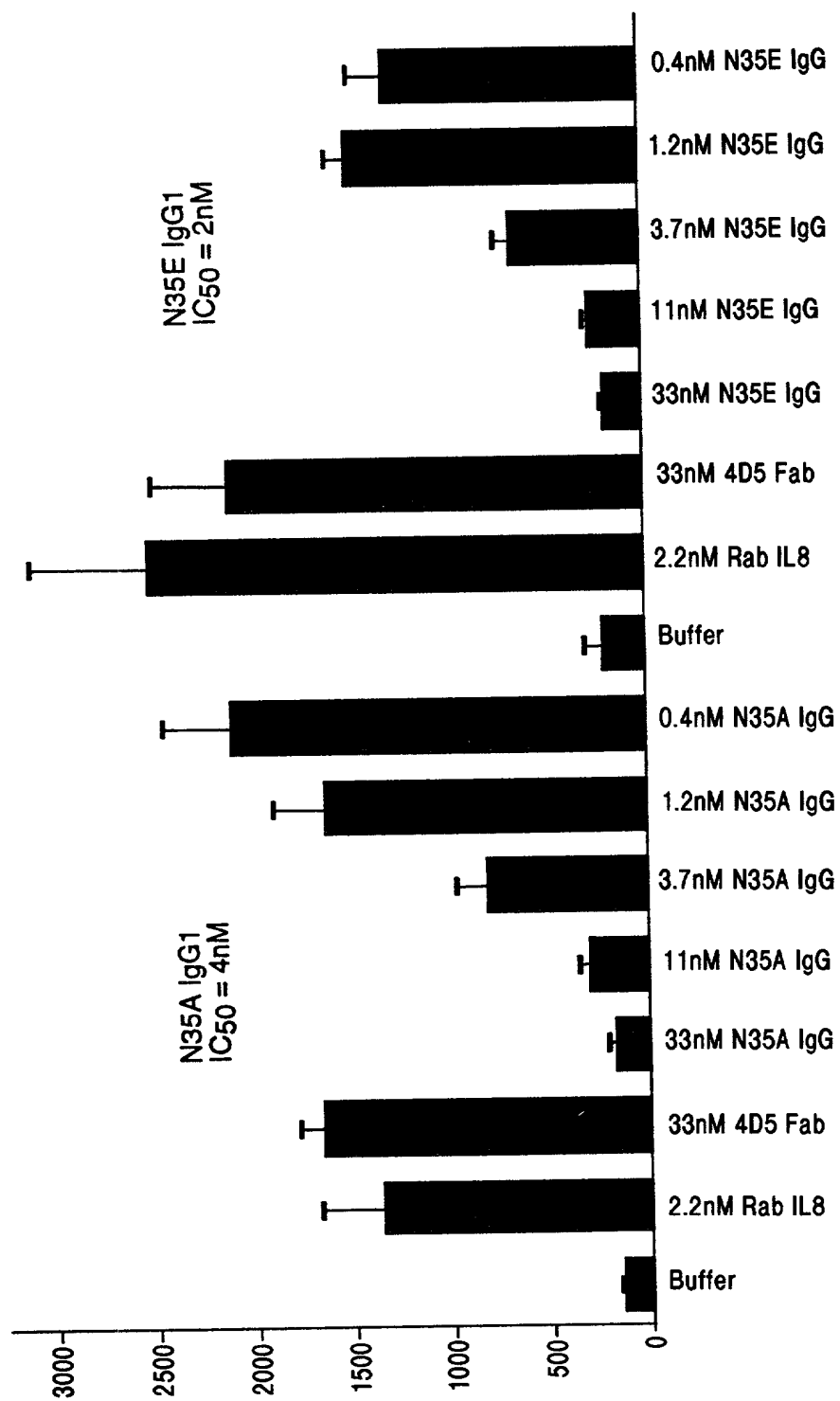
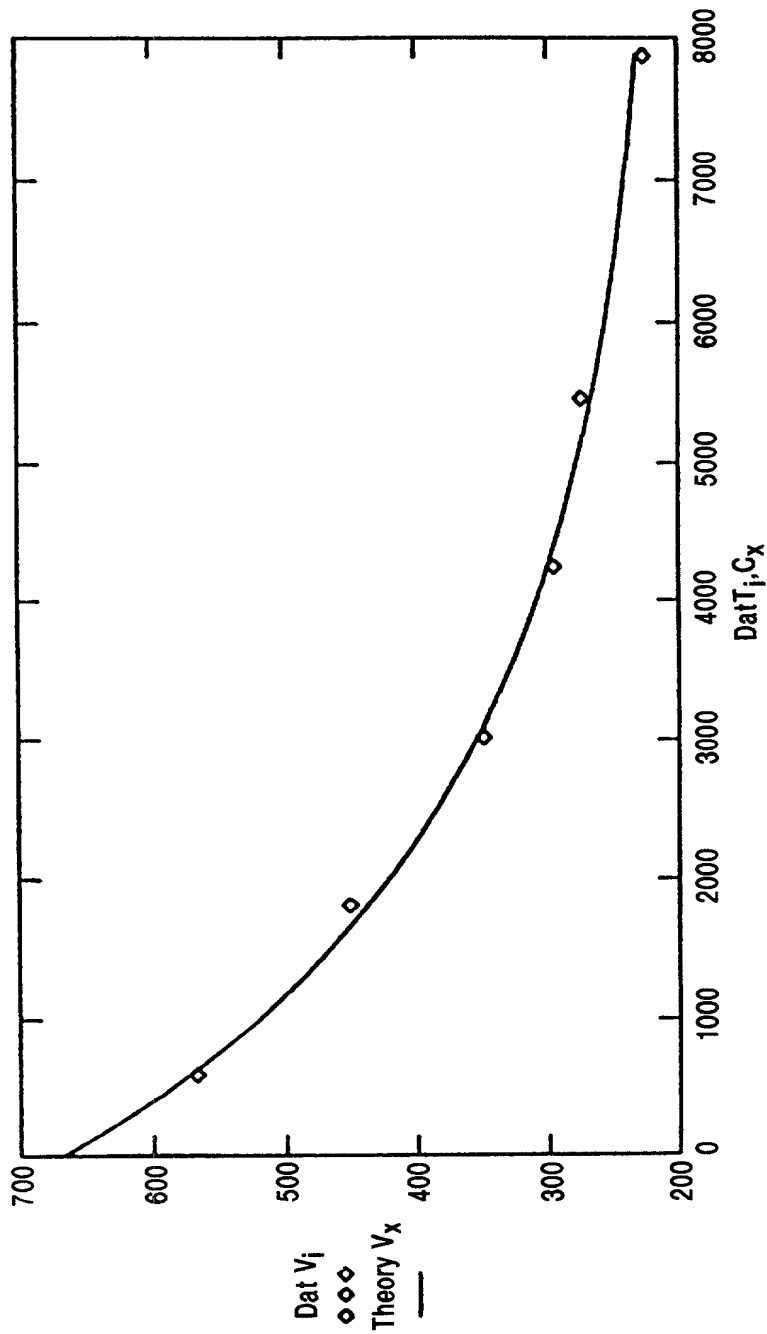


FIG. 50B

FIG. 51



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.IgG1

SAMPLE	ka	kd	Kd
Murine 6G4.2.5 IgG2a	8.3x10 ⁵	2.9x10 ⁻⁴	350pM
6G4V11N35A-IgG1	8.7x10 ⁵	7.7x10 ⁻⁵	88pM
6G4V11N35E-IgG1	3.0x10 ⁶	1.4x10 ⁻⁴	49pM

FIG. 51

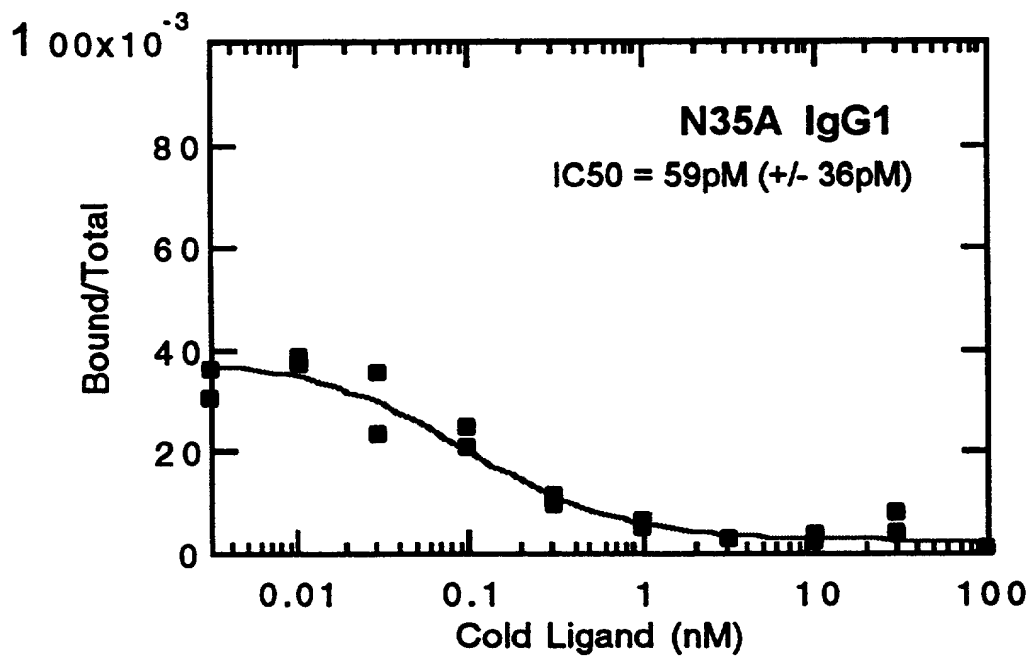


FIG. 52A

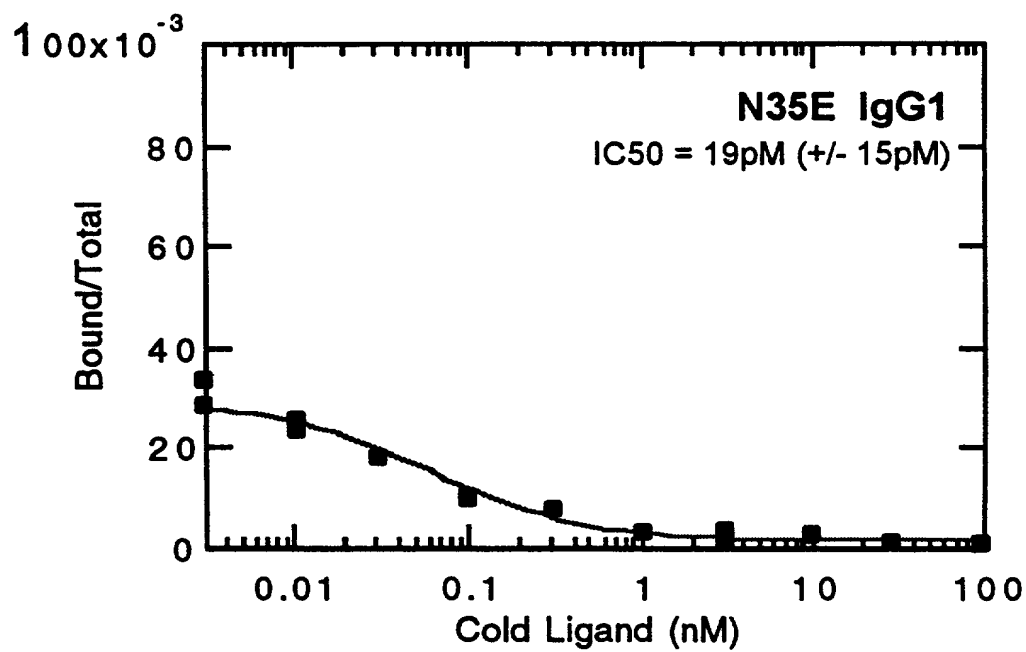


FIG. 52B

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
 TTTTCCCATA GATCTCCAAC TCCACTAAAA TACTTTTTCT TATAGCGTAA AGAAGAACGT
 -1 M K K N I A F L L A
 841 TCTATGTTTCG TTTTCTCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT
 AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
 -11 S M F V F S I A T N A Y A E V Q L V Q S
 901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
 CCGCCACCGG ACCACGTCGG TCCCCGAGT GAGGCAACA GGACACGTCG AAGACCGATG
 8 G G G L V Q P G G S L R L S C A A S G Y
 961 TCCTTCTCGA GTCACTATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
 AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTTCC GGACCTTACC
 28 S F S S H Y M H W V R Q A P G K G L E W
 1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
 CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
 48 V G Y I D P S N G E T T Y N O K F K G R
 1081 TTCACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
 AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
 68 F T L S R D N S K N T A Y L Q M N S L R
 1141 GCTGAGGACA CTGCCGTCTA TTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
 CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCTAA TAGCGATGTT ACCACTGACC
 88 A E D T A V Y Y C A R G D Y R Y N G D W
 1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
 AAGAAGCTGC AGACCCAGT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCCG
 108 F F D V W G Q G T L V T V S S A S T K G
 1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
 GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC
 128 P S V F P L A P S S K S T S G G T A A L
 1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
 CCGACGGACC AGTTCTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
 148 G C L V K D Y F P E P V T V S W N S G A
 1381 CTGACCAGCG GCGTGCACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTA CTACTCCCTC
 GACTGGTTCG CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG
 168 L T S G V H T F P A V L Q S S G L Y S L
 1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
 TCGTCGCACC ACTGGCACGG GAGGTCGTCG AACCCGTGGG TCTGGATGTA GACGTTGCAC
 188 S S V V T V P S S S L G T Q T Y I C N V
 1501 AATCACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
 TTAGTGTTTCG GGTGCTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
 208 N H K P S N T K V D K K V E P K S C D K
 1561 ACTCACACAT GCCCGCCGTGA
 TGAGTGTGTA CGGGCGGCACT
 228 T H T C P P O

FIG. 53

FIG. 54A is a line graph showing the relative binding of various antibodies to IL-8. The y-axis represents the ratio of bound to total antibody (Bound/Total), ranging from 0.0 to 0.7. The x-axis represents the concentration of the antibody competitor in nanomolar (nM), on a logarithmic scale from 10⁻² to 10³. The graph displays several curves, each corresponding to a different antibody or competitor. The curves generally show a decrease in the Bound/Total ratio as the competitor concentration increases, indicating competitive inhibition. The legend identifies the curves: IL-8 (dashed line), Fab 27328-48 (solid line), Fab 27328-79 (dotted line), Fab-PEG5 (dash-dot line), Fab-PEG10 (dotted line), Fab-PEG20 (solid line), and an average (Avg) curve (dashed line). The IC50 values for each curve are listed in the table below.

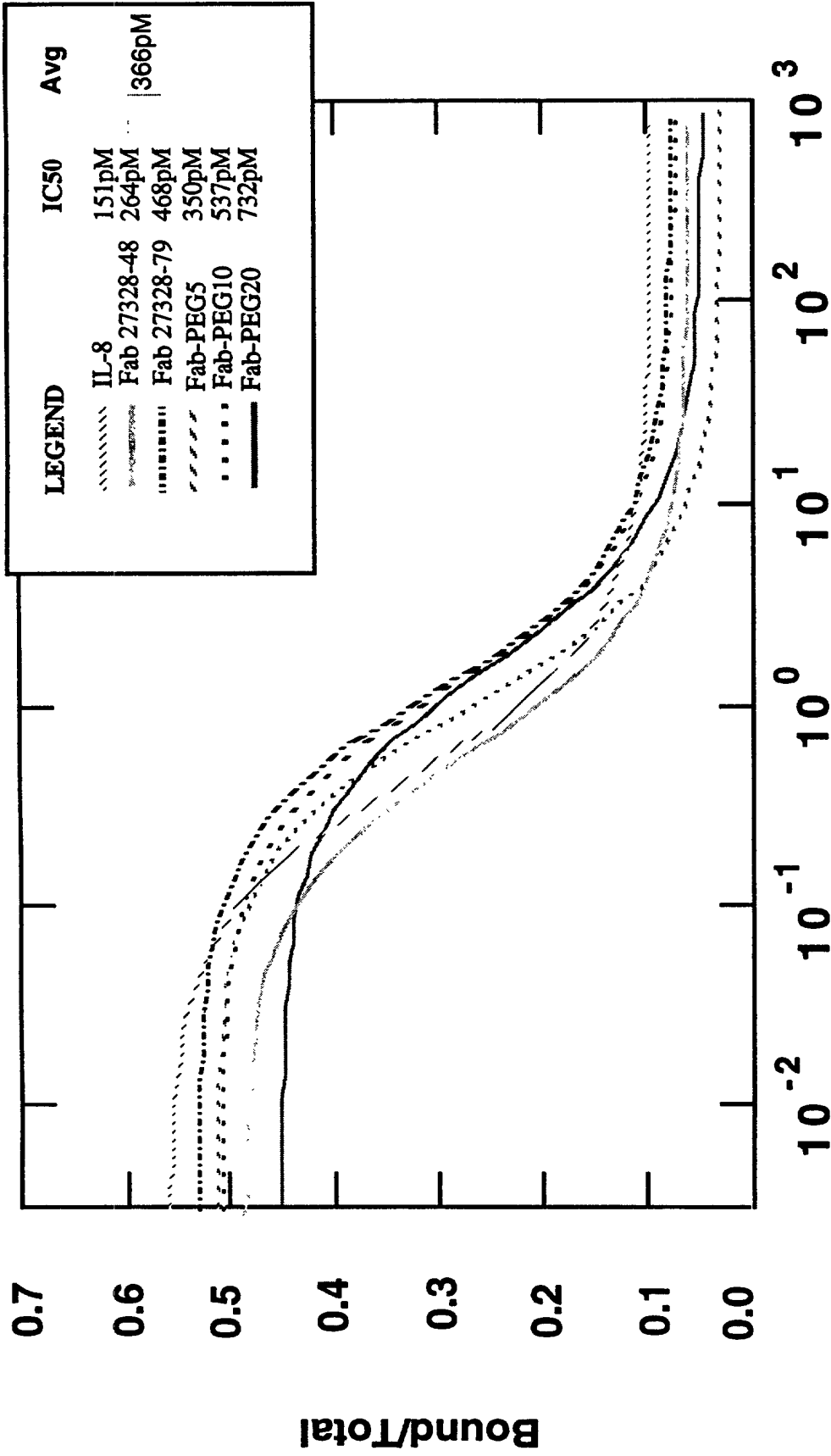
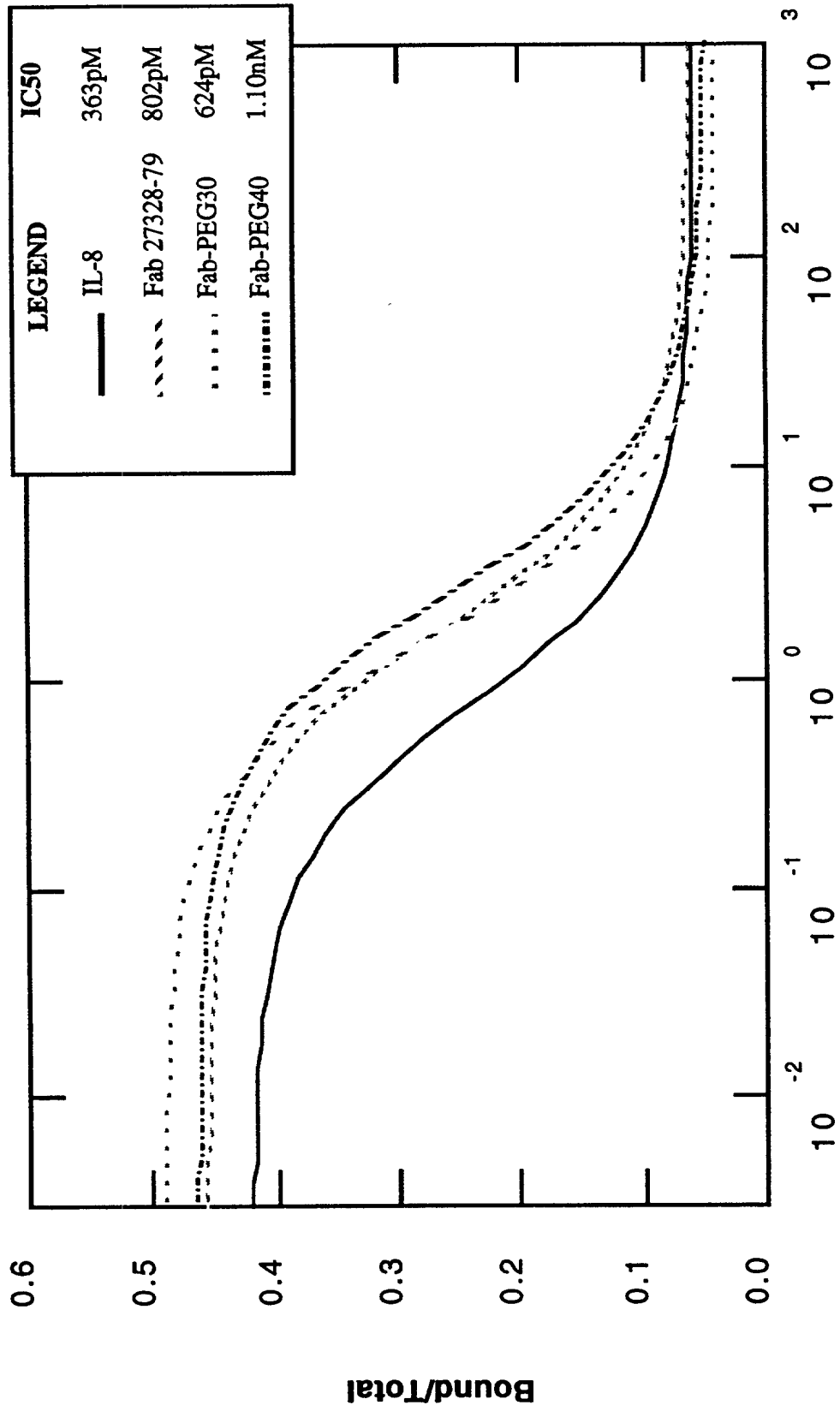


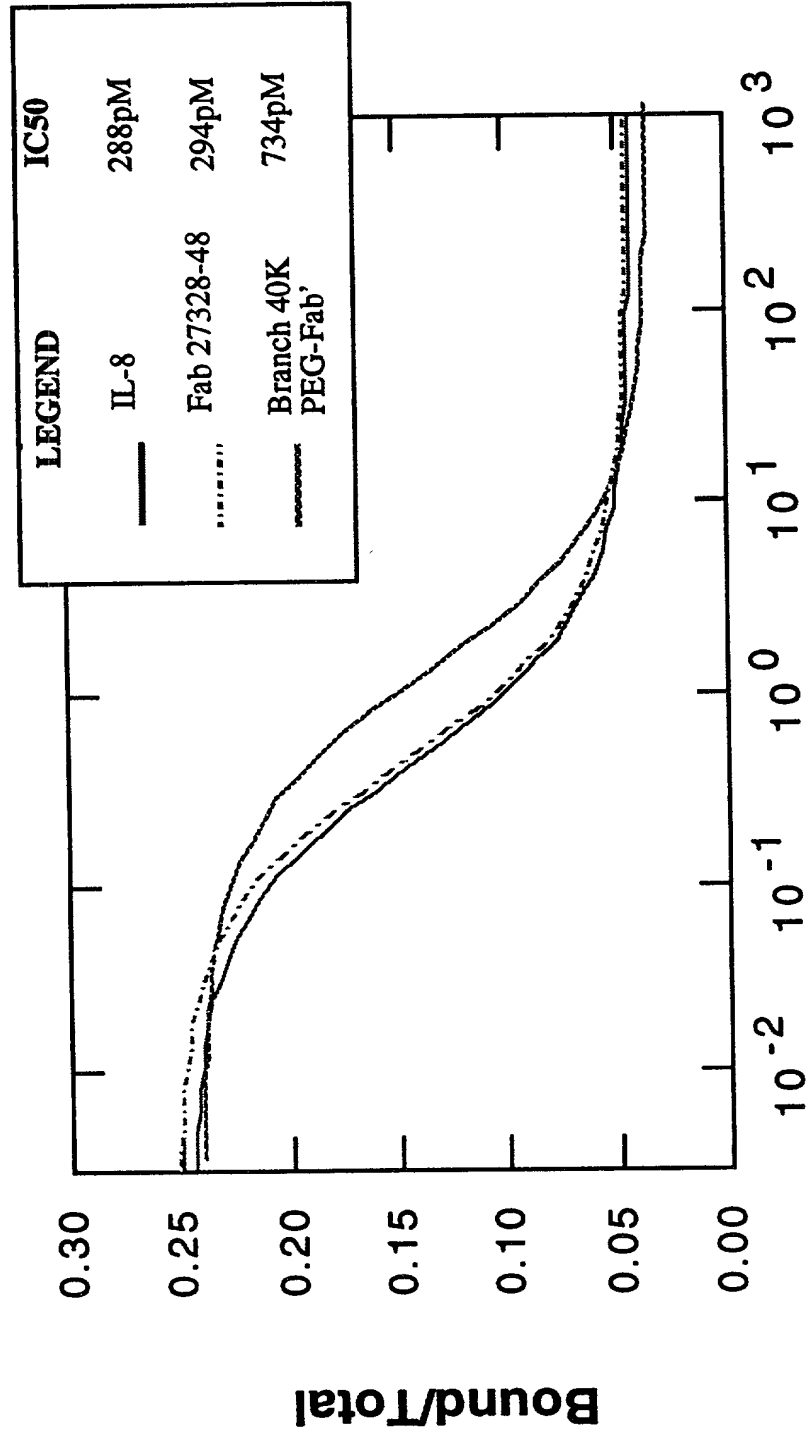
FIG. 54A

FIG. 54B is a line graph showing the relative binding of various antibodies to IL-8. The y-axis represents the ratio of bound to total antibody (Bound/Total), ranging from 0.0 to 0.6. The x-axis represents the concentration of the antibody competitor in nanomolar (nM), ranging from 10⁻² to 10³. Four curves are shown, each corresponding to a different antibody: IL-8 (solid line), Fab 27328-79 (dashed line), Fab-PEG30 (dotted line), and Fab-PEG40 (dash-dot line). The IL-8 curve shows the highest binding, reaching a plateau of approximately 0.55 at 10³ nM. The Fab 27328-79 curve reaches a plateau of approximately 0.45. The Fab-PEG30 curve reaches a plateau of approximately 0.4. The Fab-PEG40 curve reaches a plateau of approximately 0.35. The curves are sigmoidal, indicating a binding affinity that increases with competitor concentration.



Antibody Competitor (nM)

FIG. 54B



Antibody Competitor (nM)

FIG. 54C

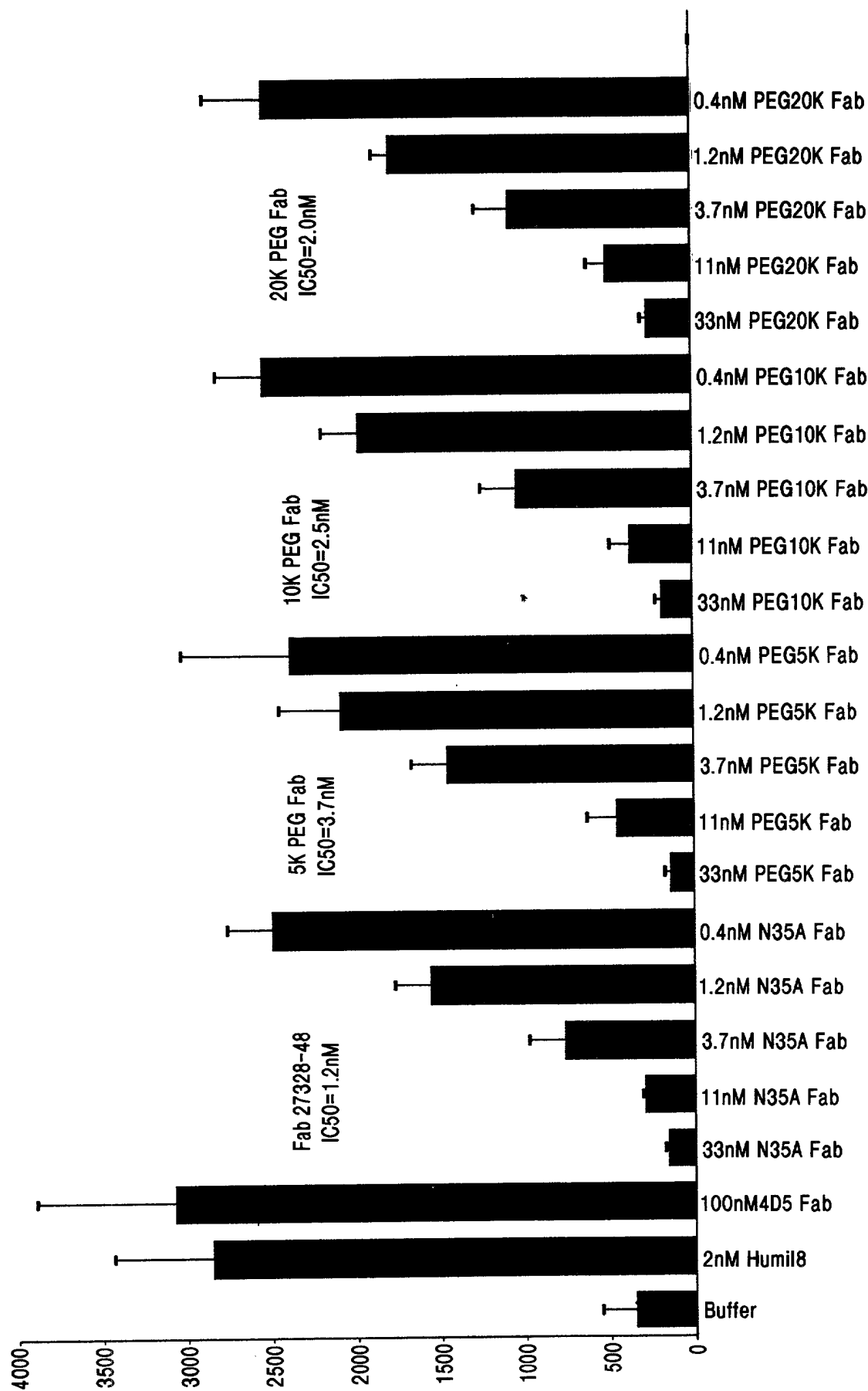


FIG. 55A

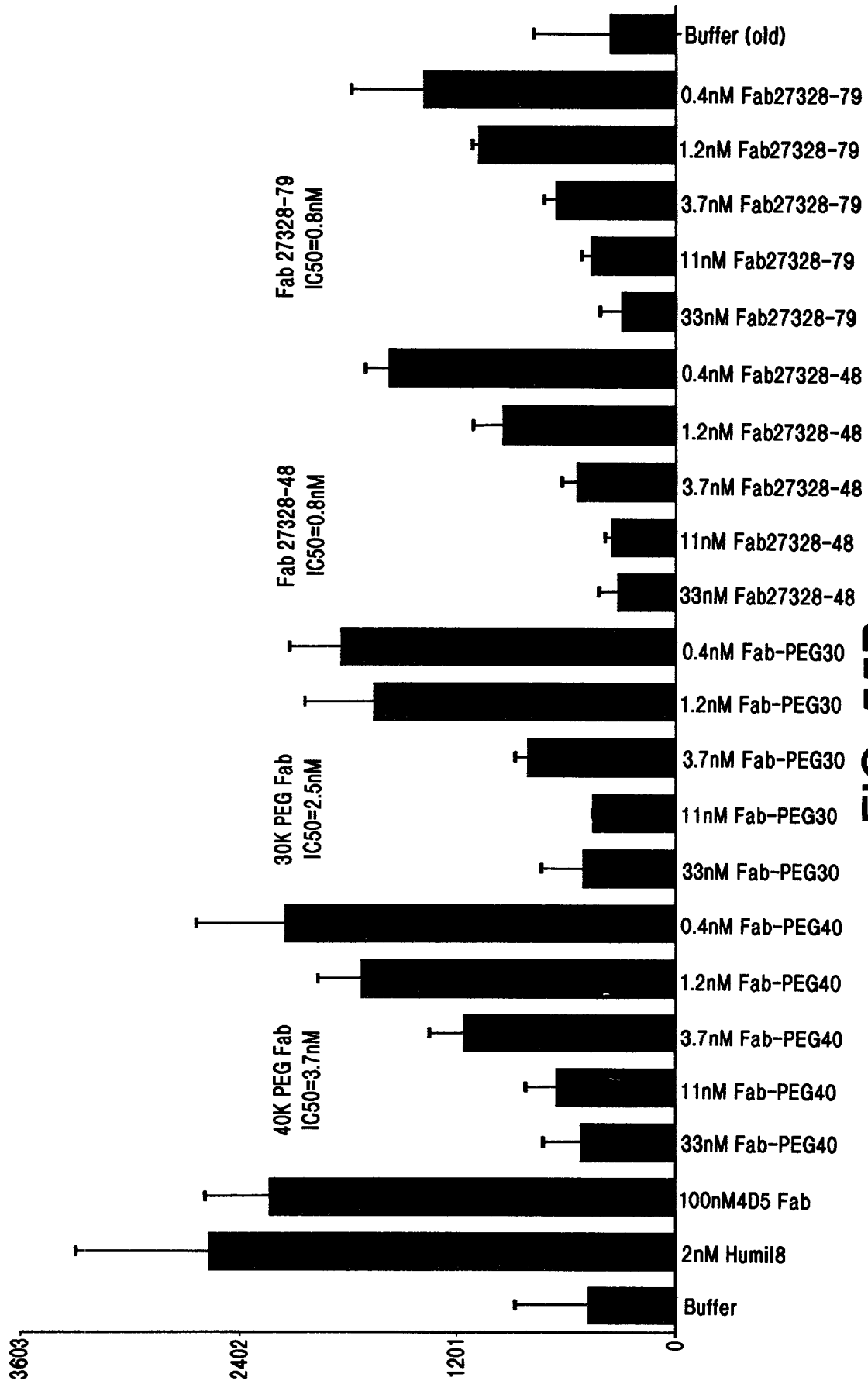


FIG. 55B

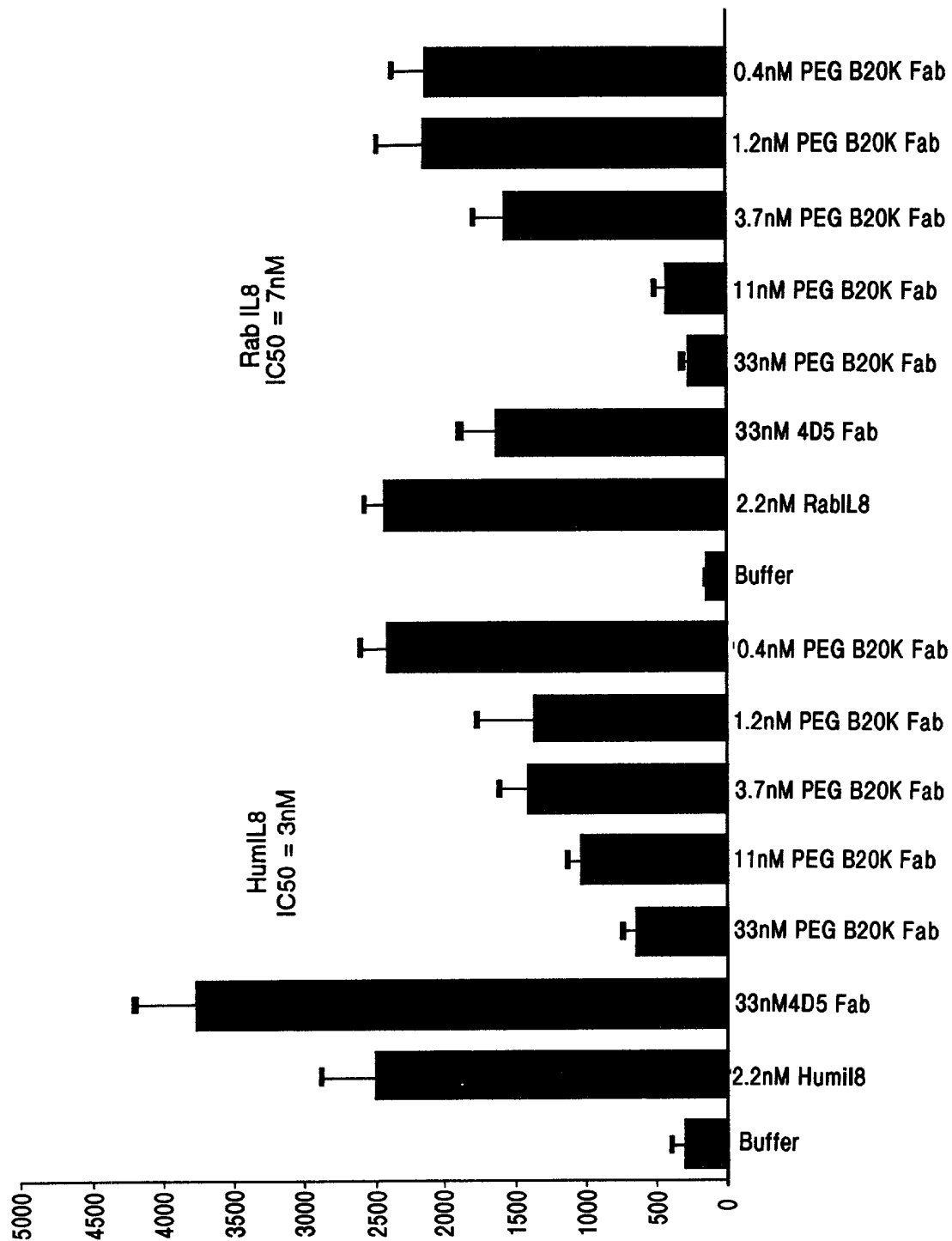
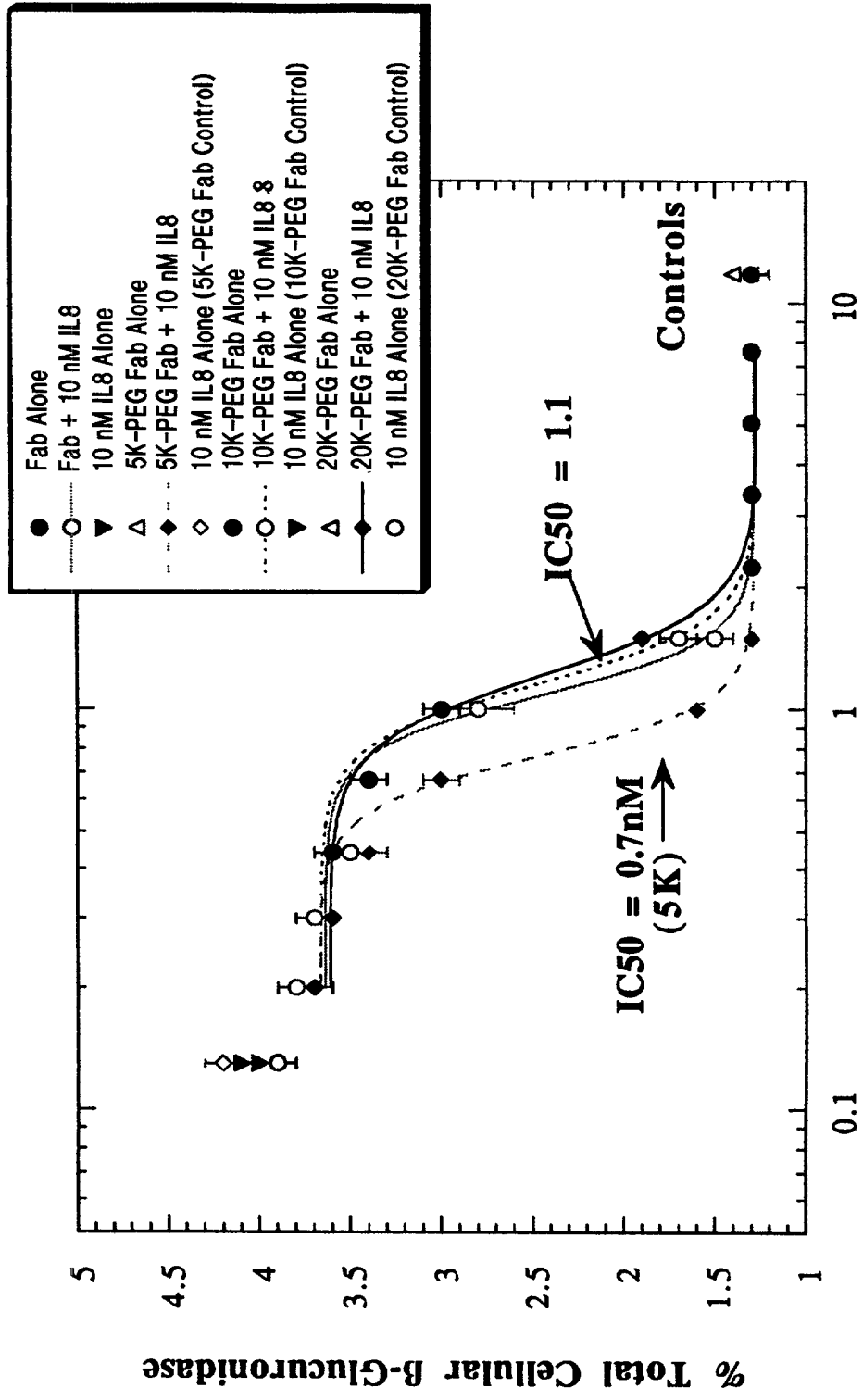


FIG. 55C

100%
 80%
 60%
 40%
 20%
 0%



Molar Ratio Antibody:IL-8
FIG. 56A

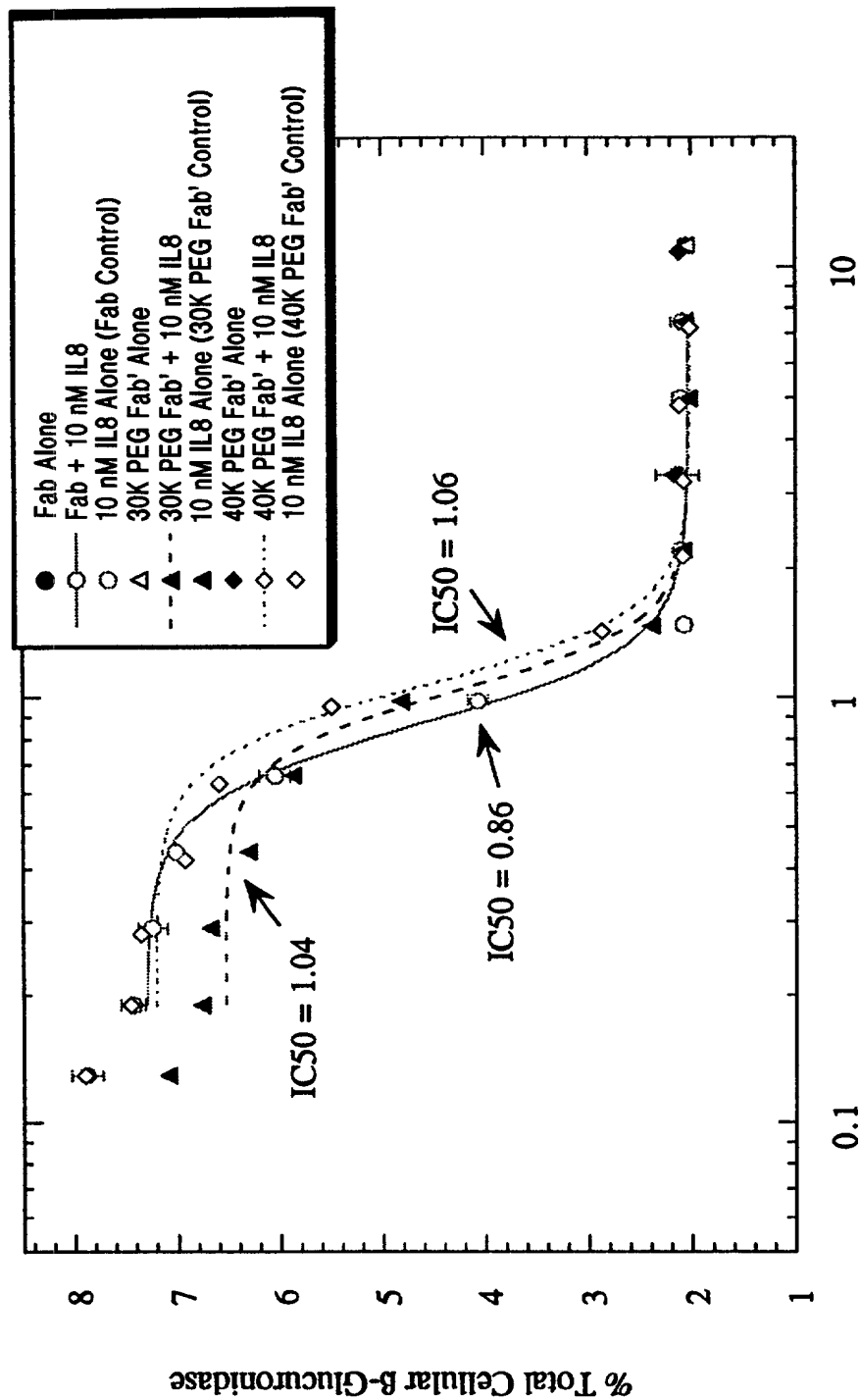
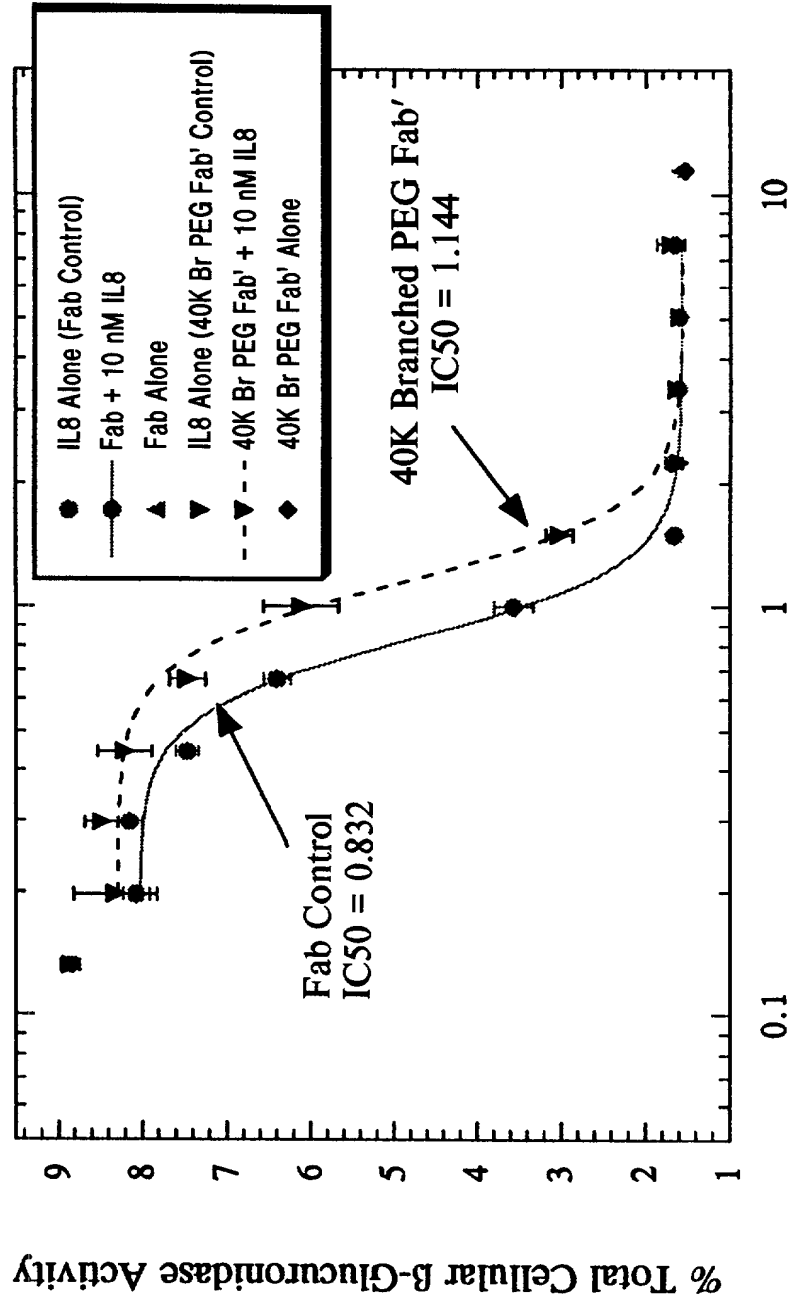
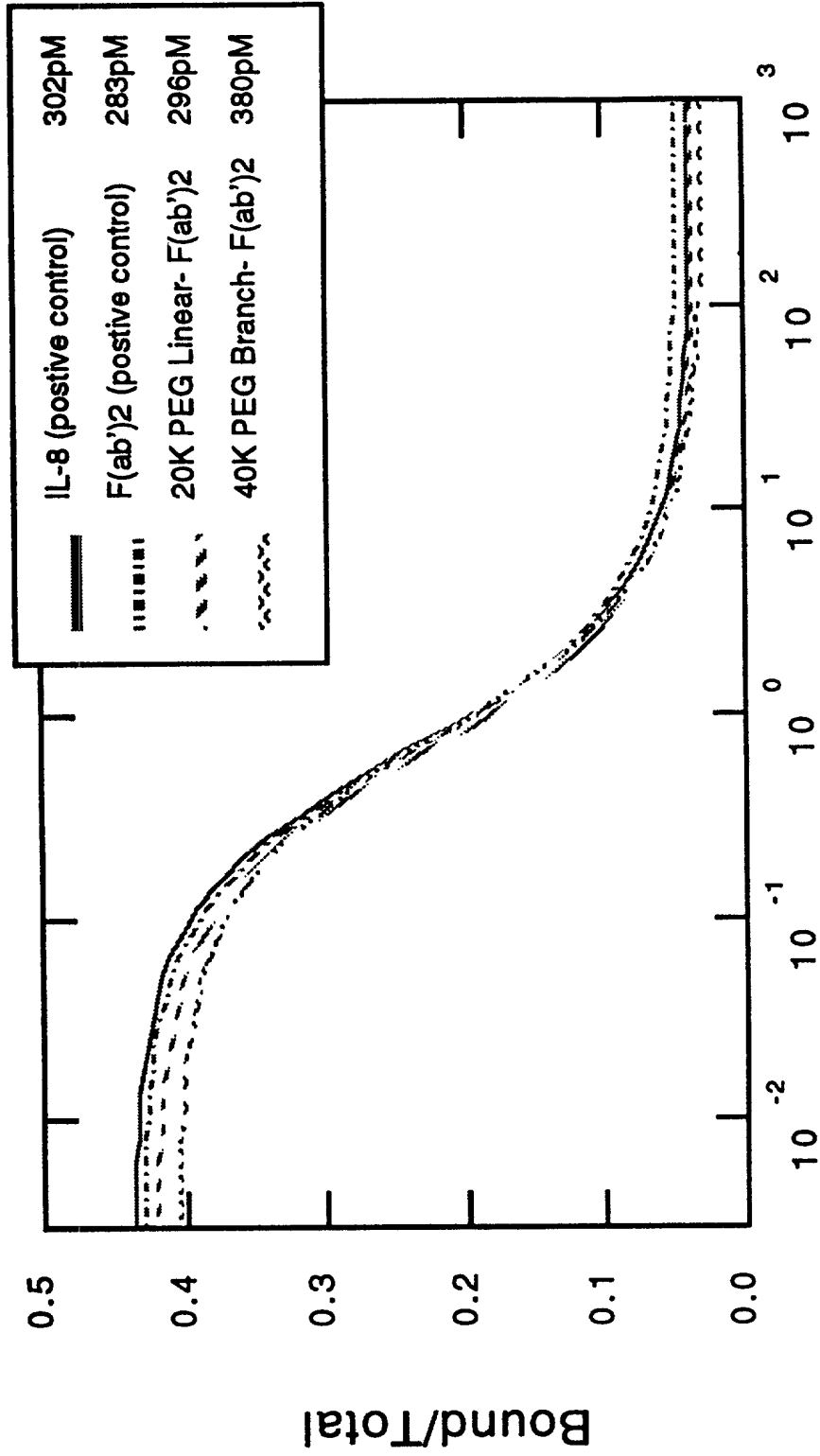


FIG. 56B



Molar Ratio Antibody:IL8

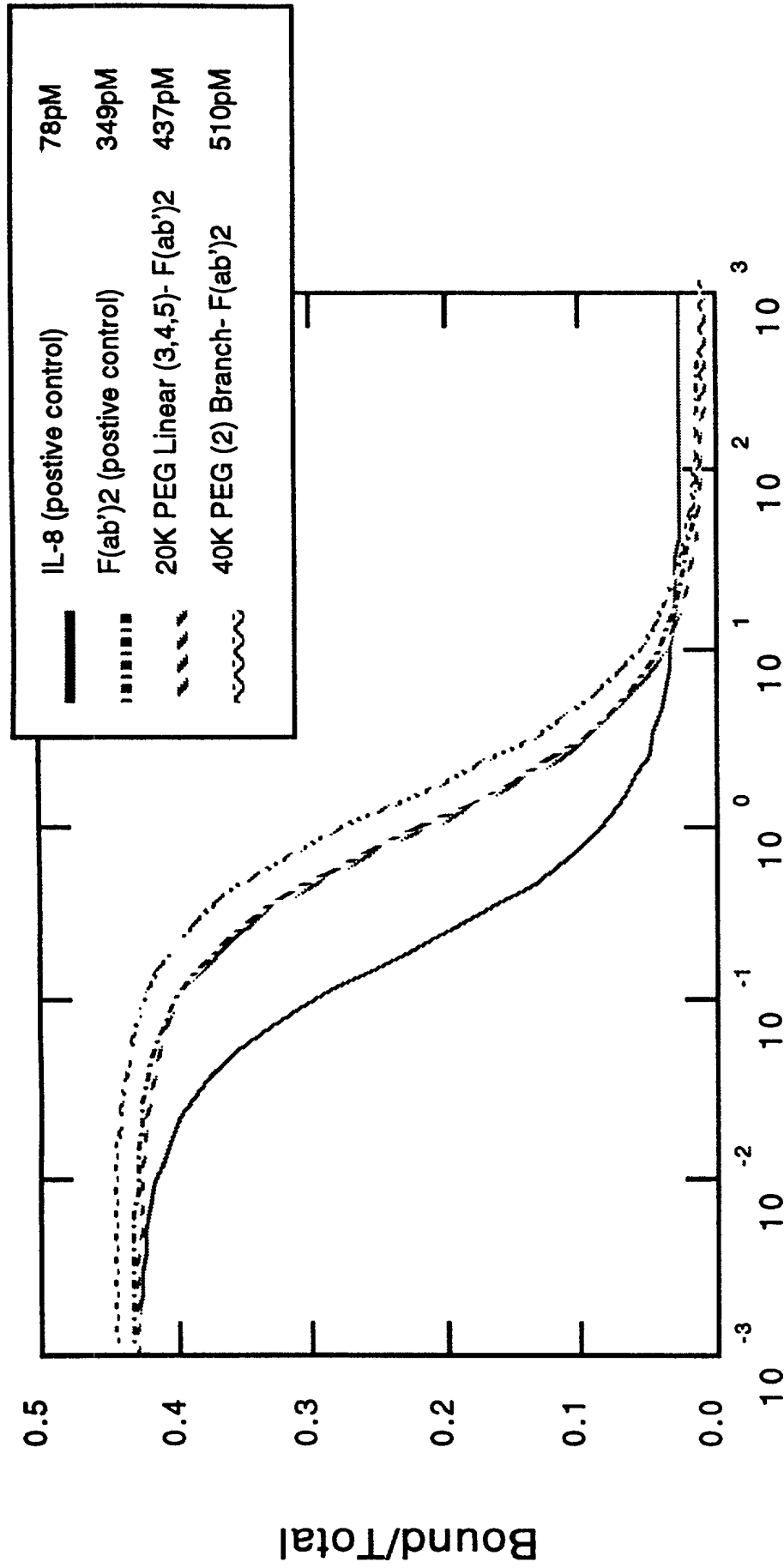
FIG. 56C



Pegylated F(ab')₂ (nM)

FIG. 57A

FIG. 57B is a line graph showing the binding of IL-8 to F(ab')₂ antibodies. The y-axis represents the ratio of bound to total antibody (Bound/Total) and the x-axis represents the concentration of IL-8 (nM). The graph shows four curves corresponding to different antibodies: IL-8 (positive control), F(ab')₂ (positive control), 20K PEG Linear (3,4,5)- F(ab')₂, and 40K PEG (2) Branch- F(ab')₂. The 20K PEG Linear (3,4,5)- F(ab')₂ curve shows the highest binding, followed by the 40K PEG (2) Branch- F(ab')₂ curve. The F(ab')₂ (positive control) curve shows intermediate binding, and the IL-8 (positive control) curve shows the lowest binding.



Pegylated F(ab')₂ (nM)
FIG. 57B

2193
 1462
 731
 0

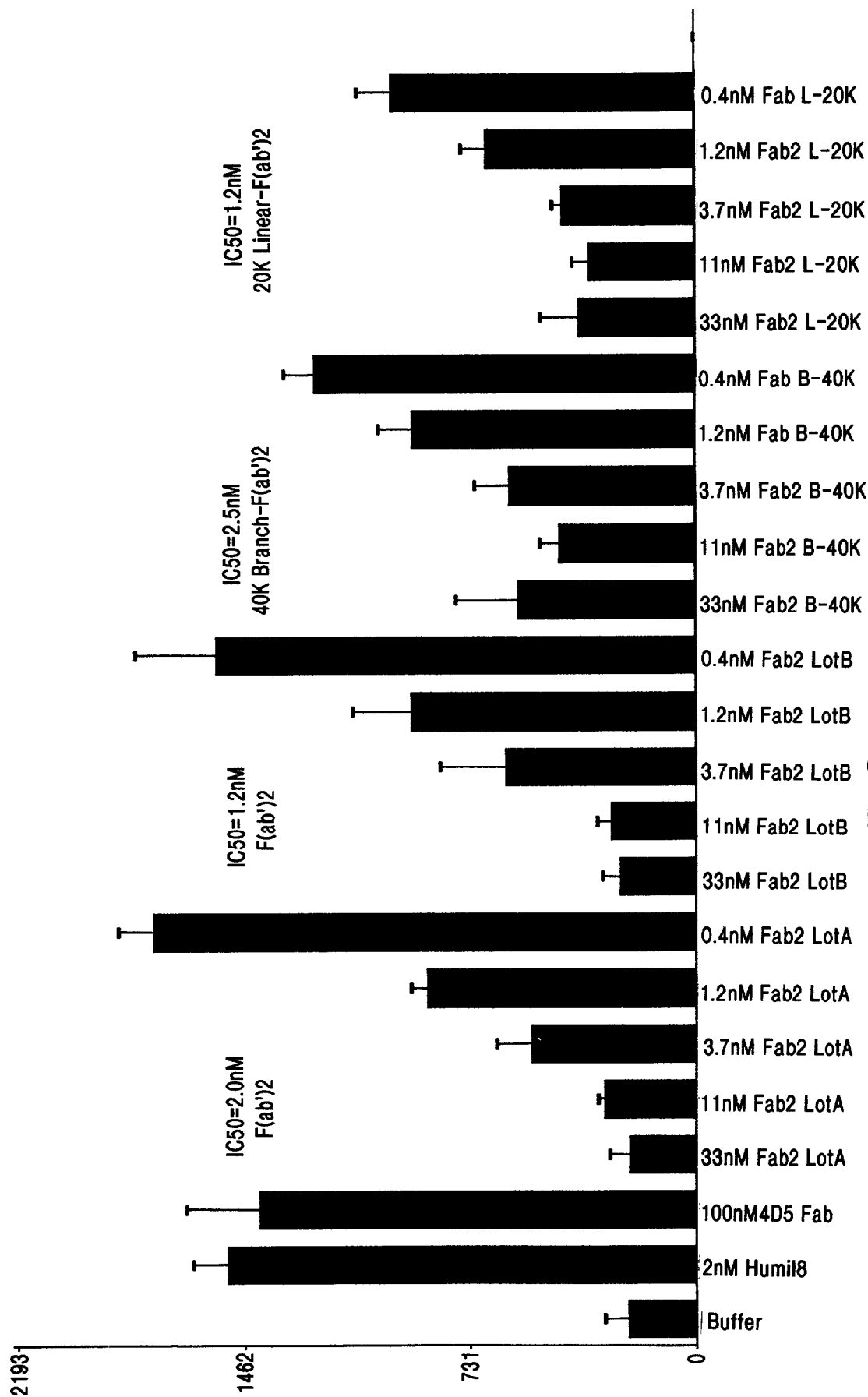


FIG. 58A

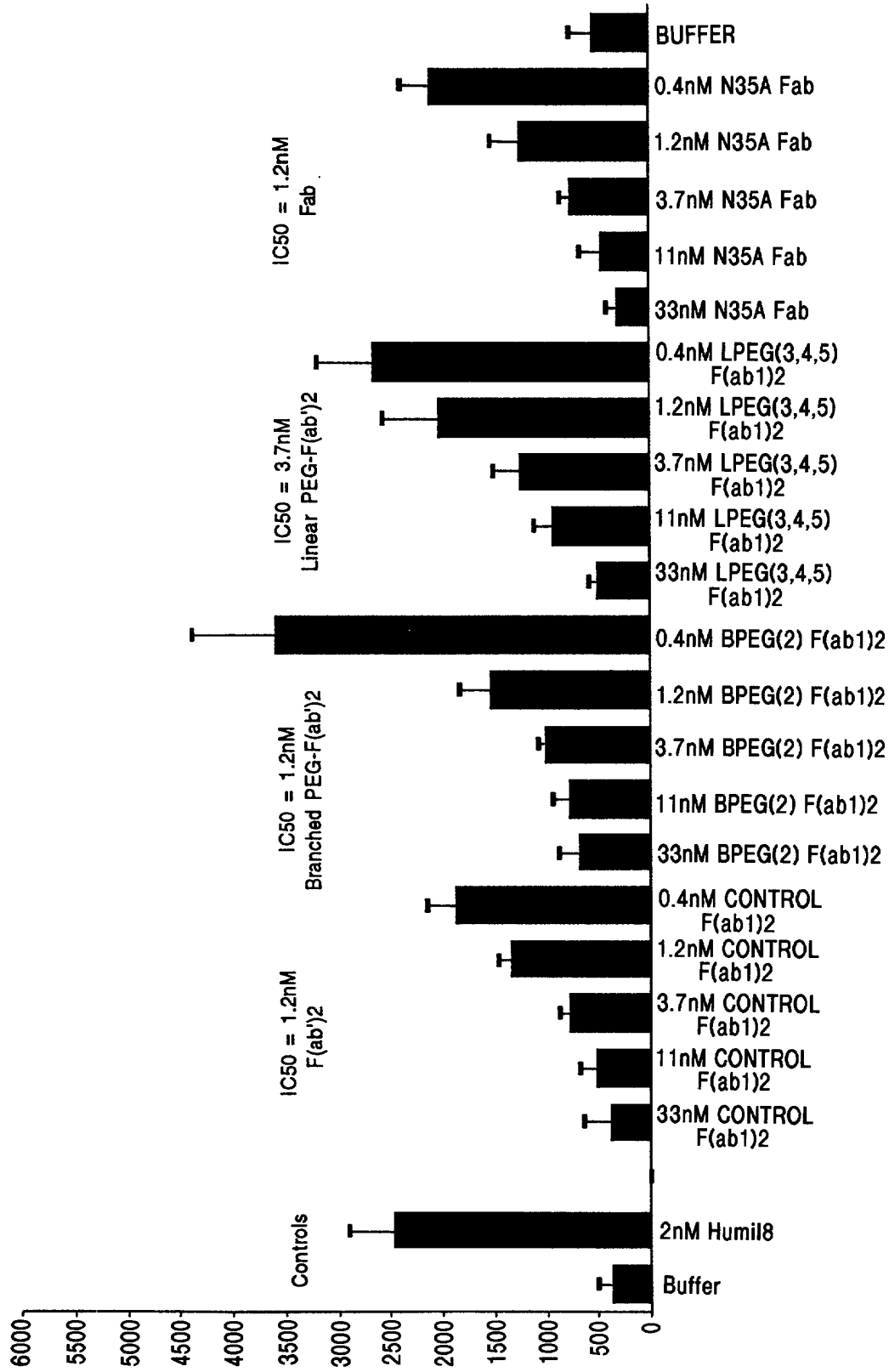
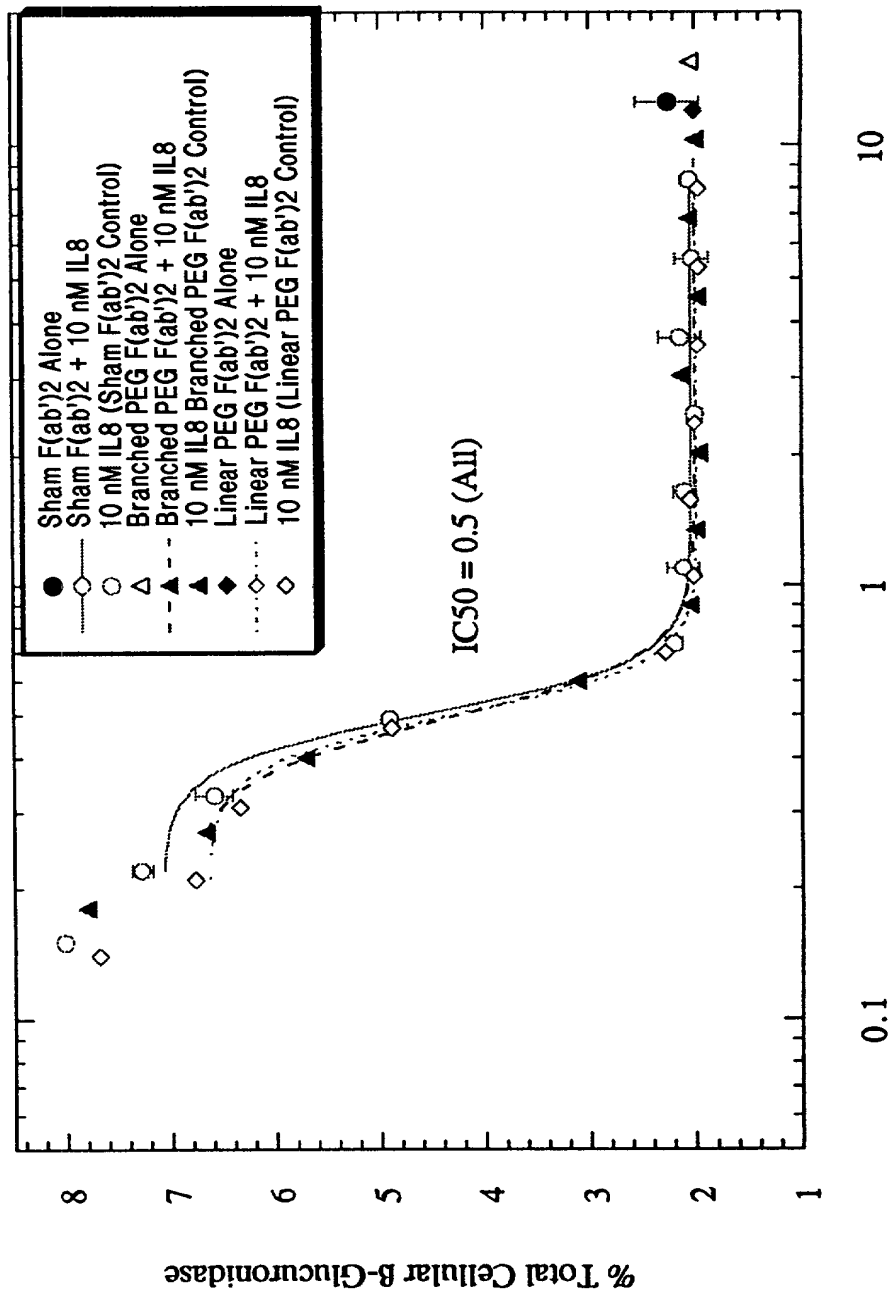
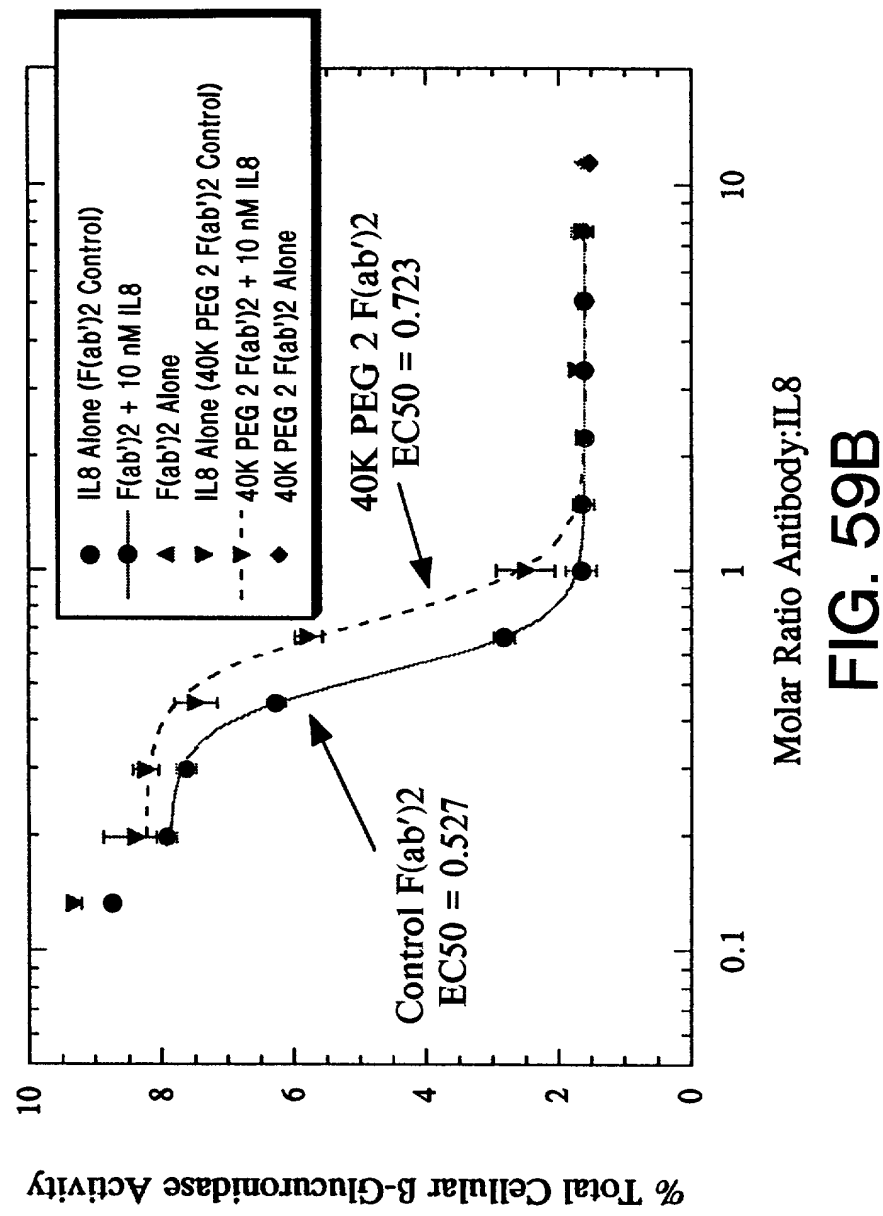


FIG. 58B



Molar Ratio Antibody:IL-8

FIG. 59A



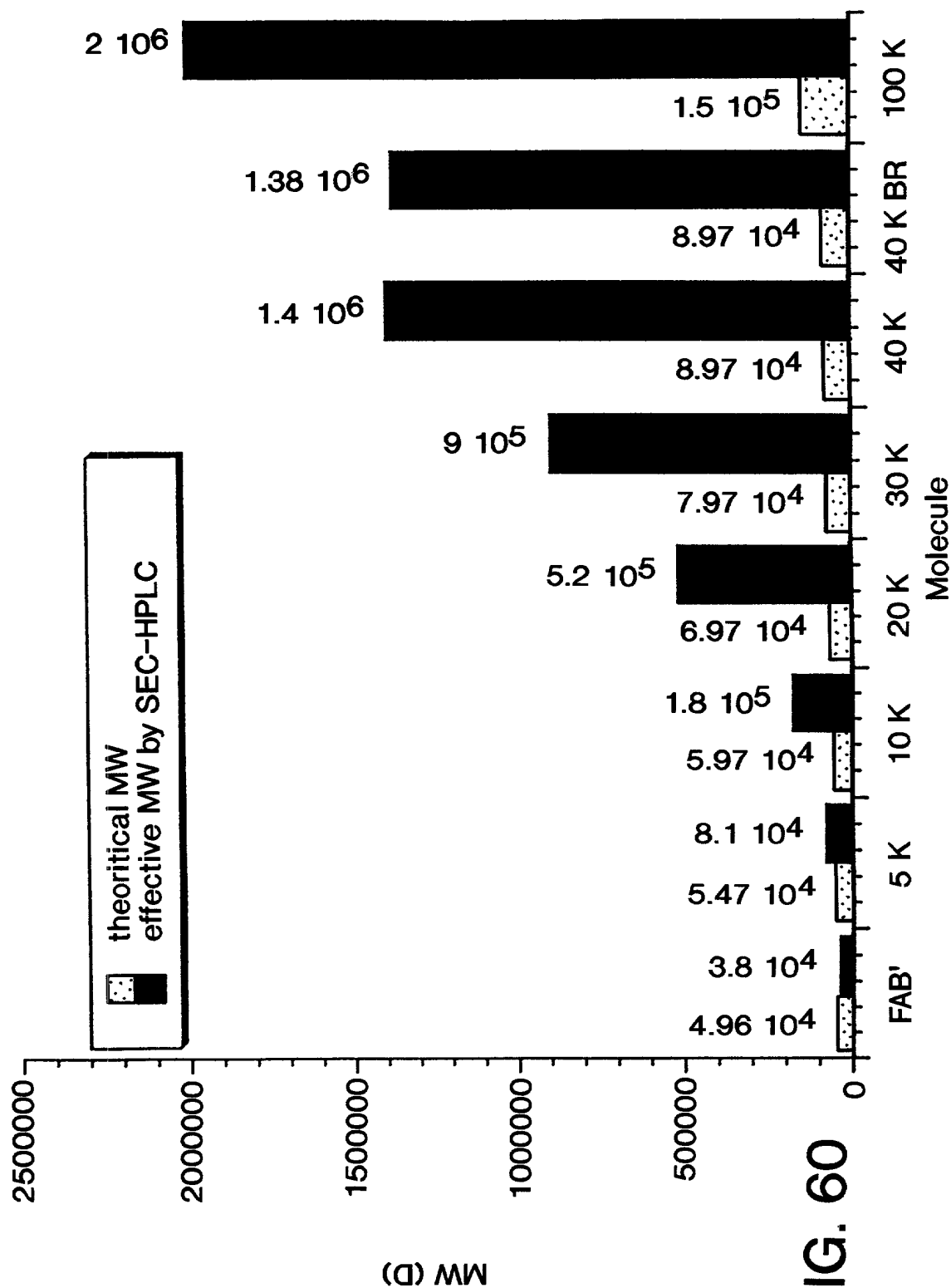


FIG. 60

FIG. 61A

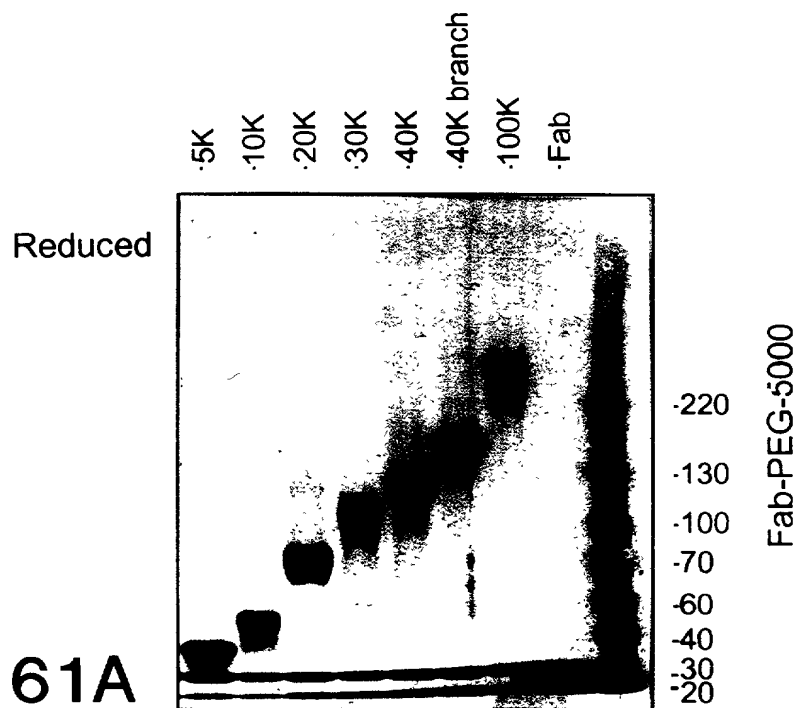
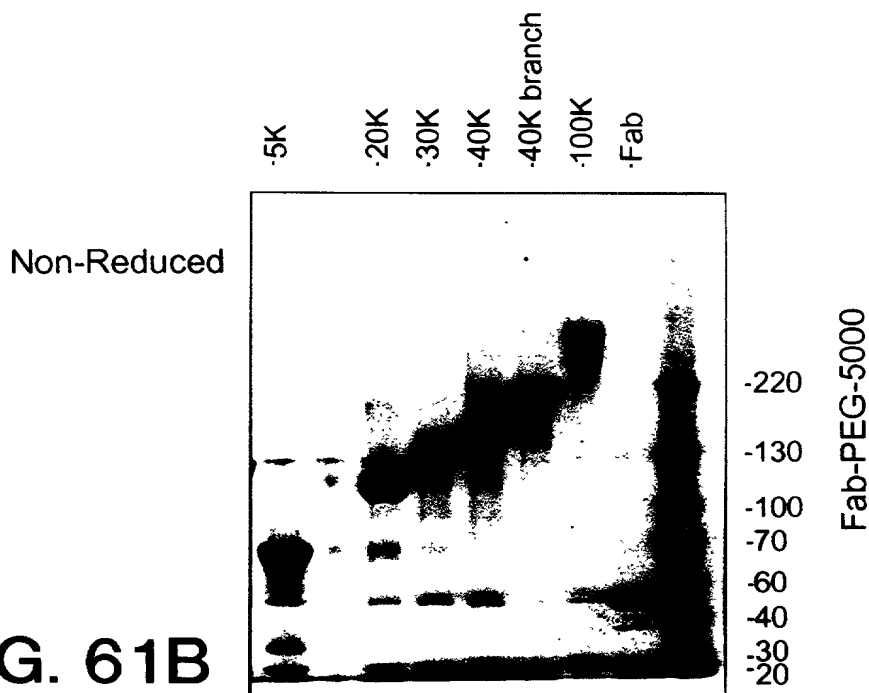


FIG. 61B



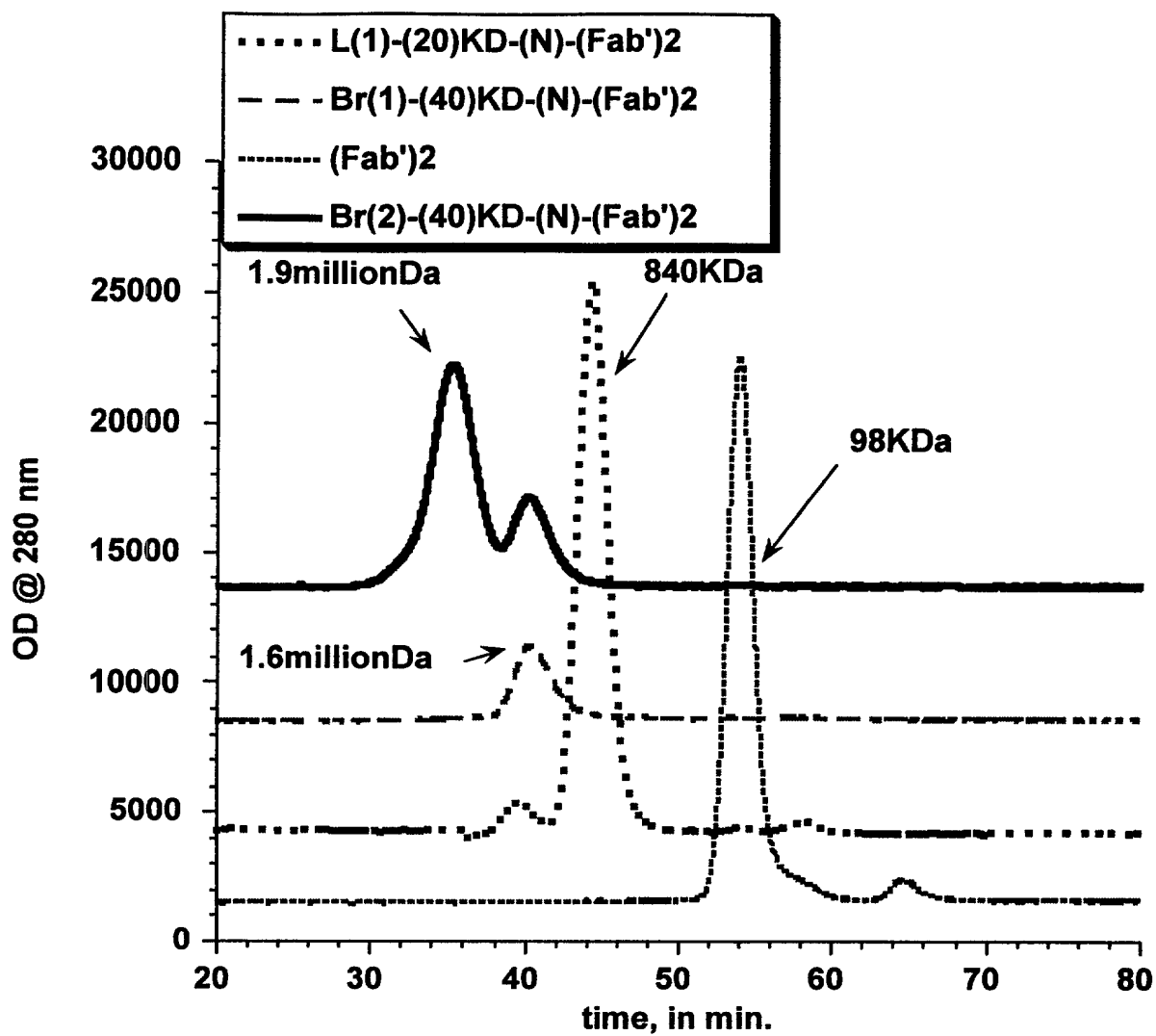


FIG. 62

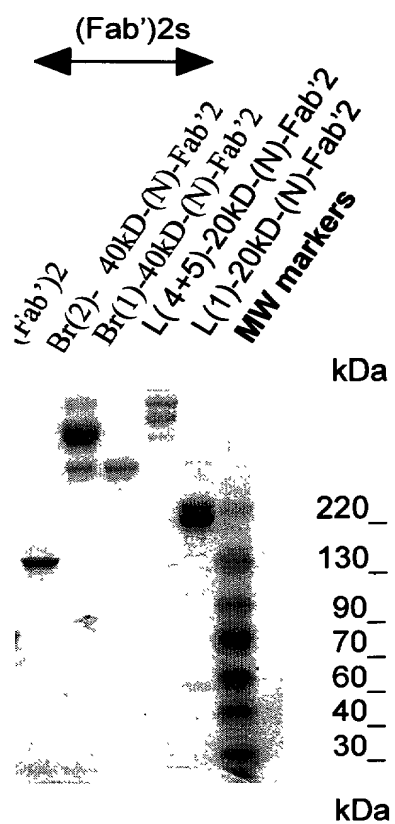


FIG. 64

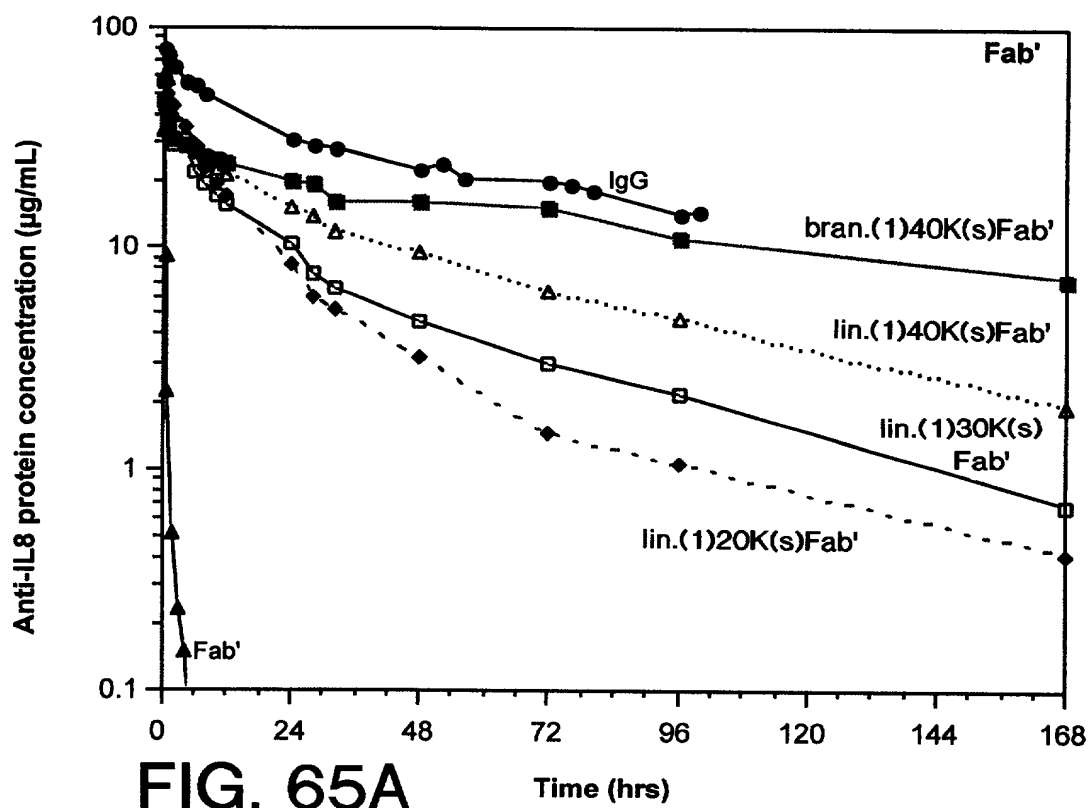


FIG. 65A

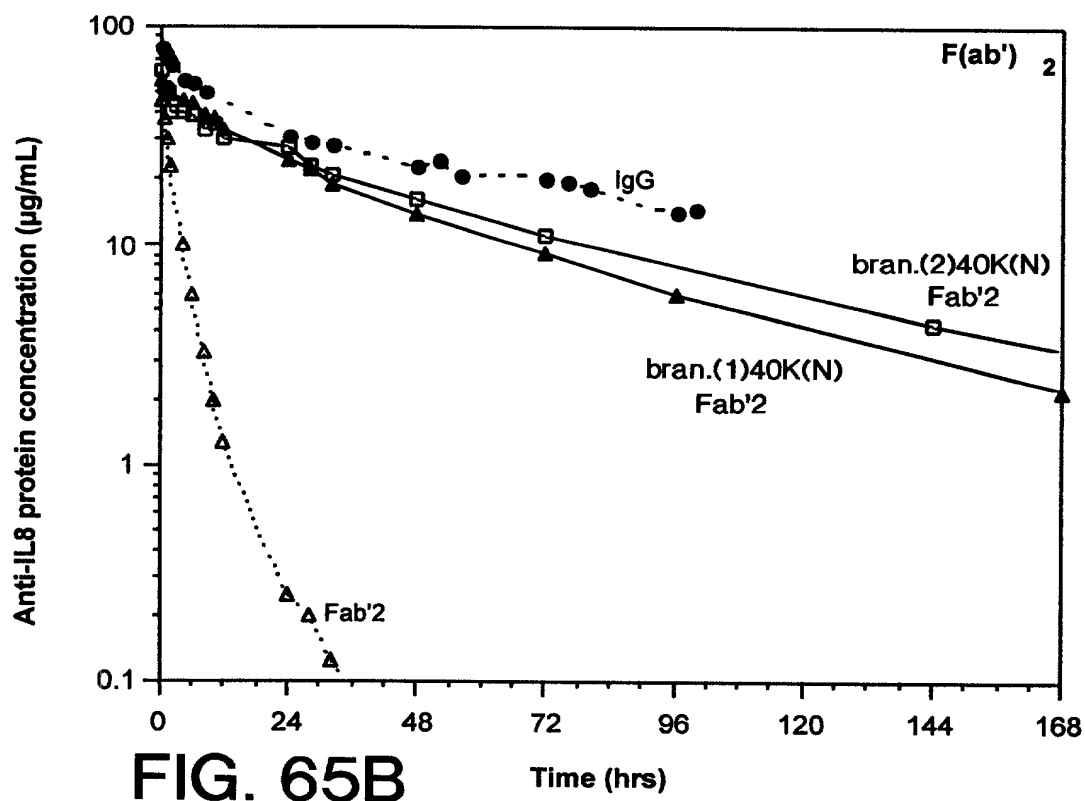


FIG. 65B

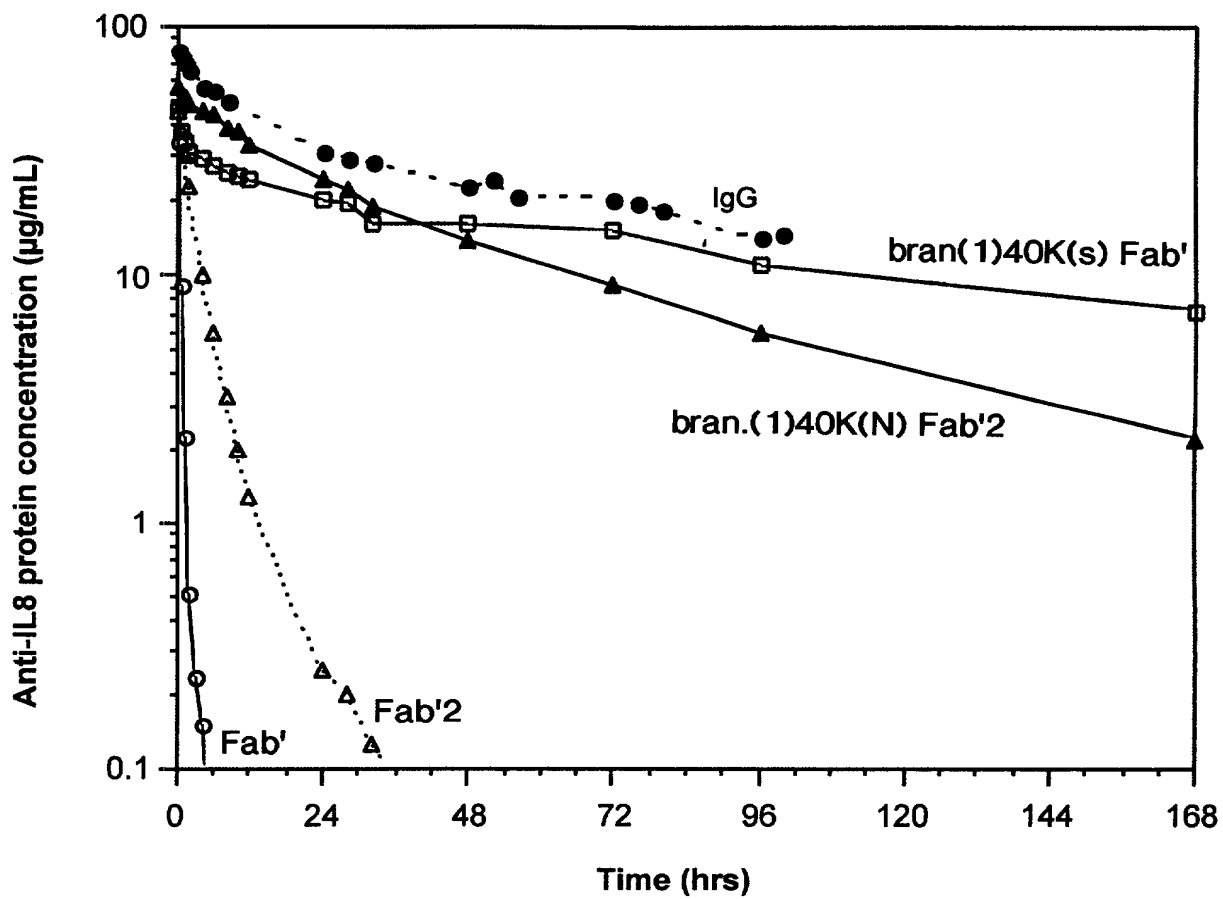


FIG. 66

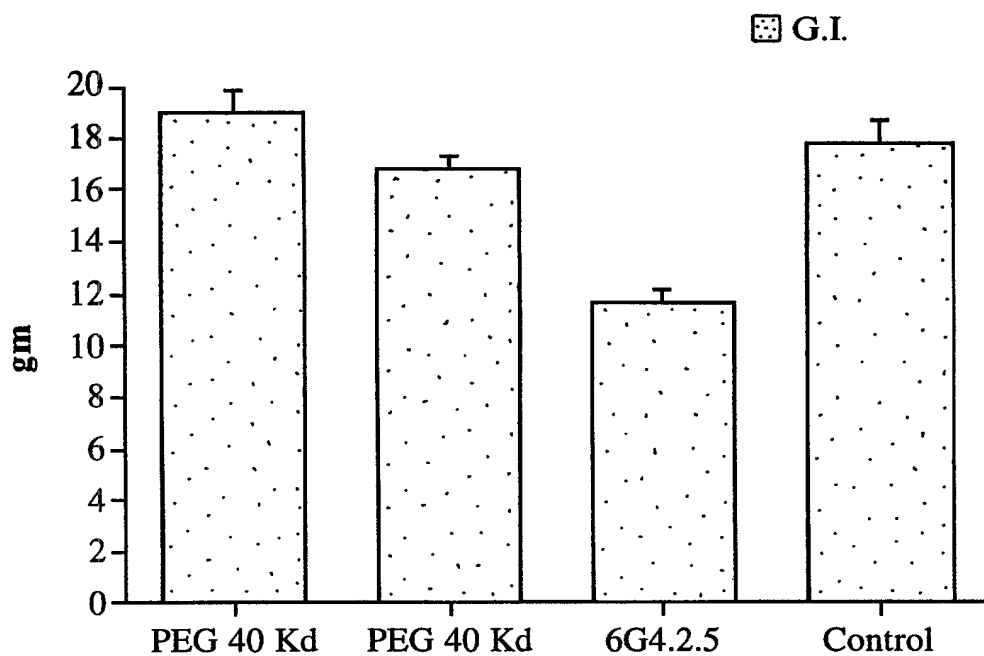


FIG. 67

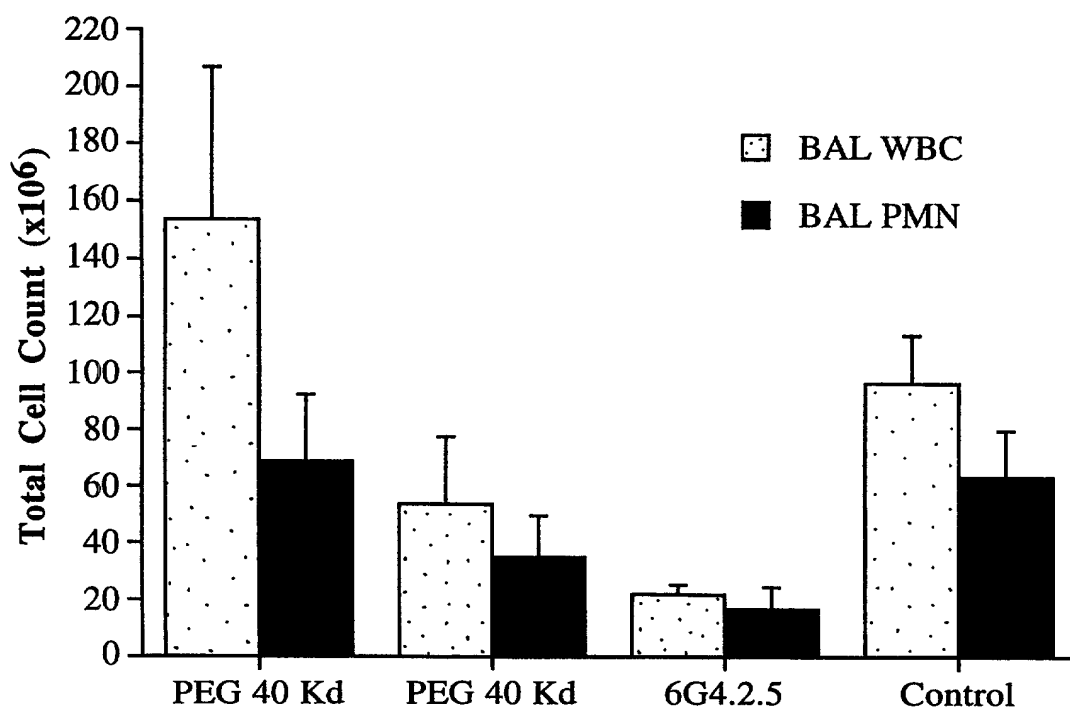


FIG. 68

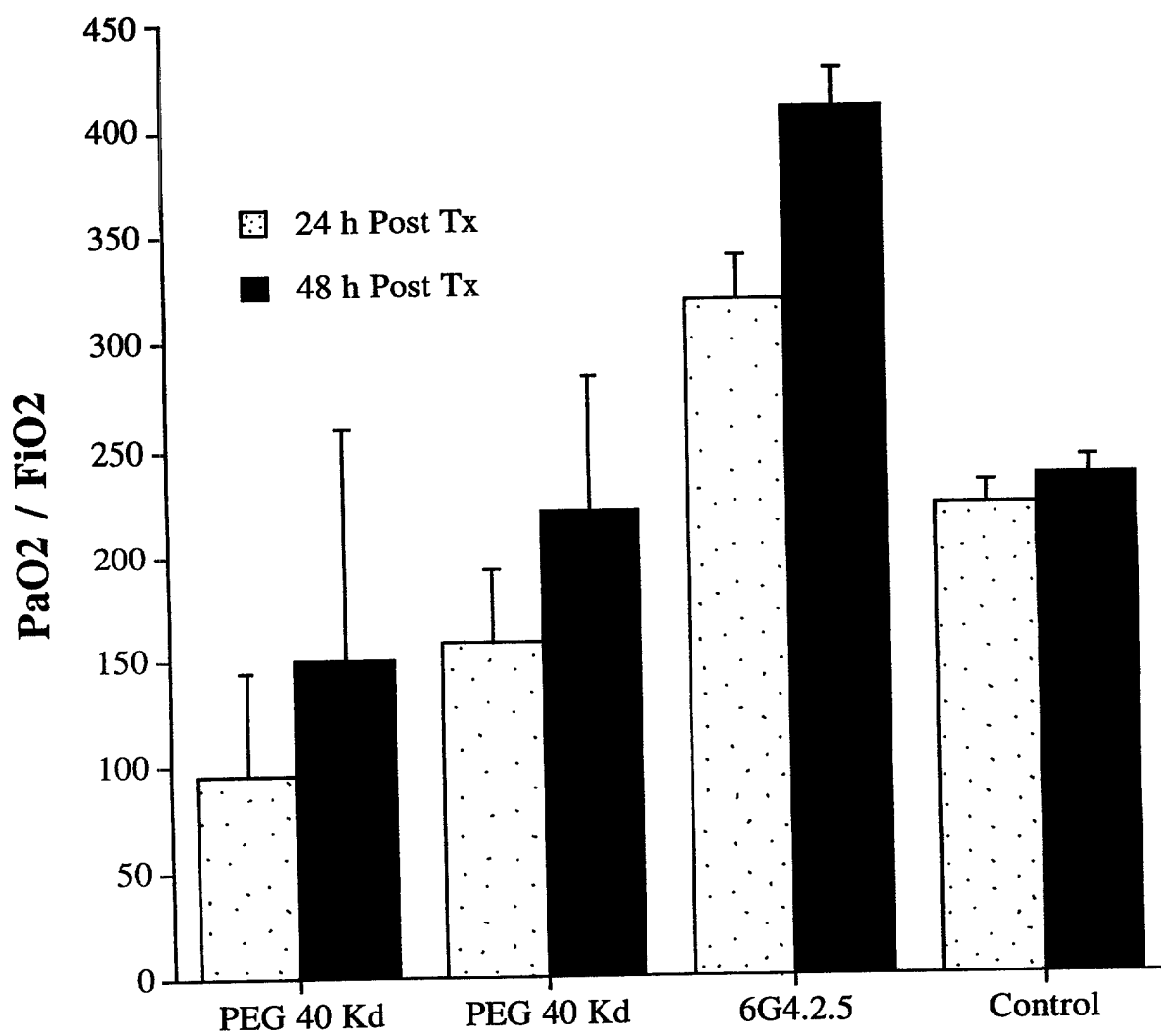


FIG. 69

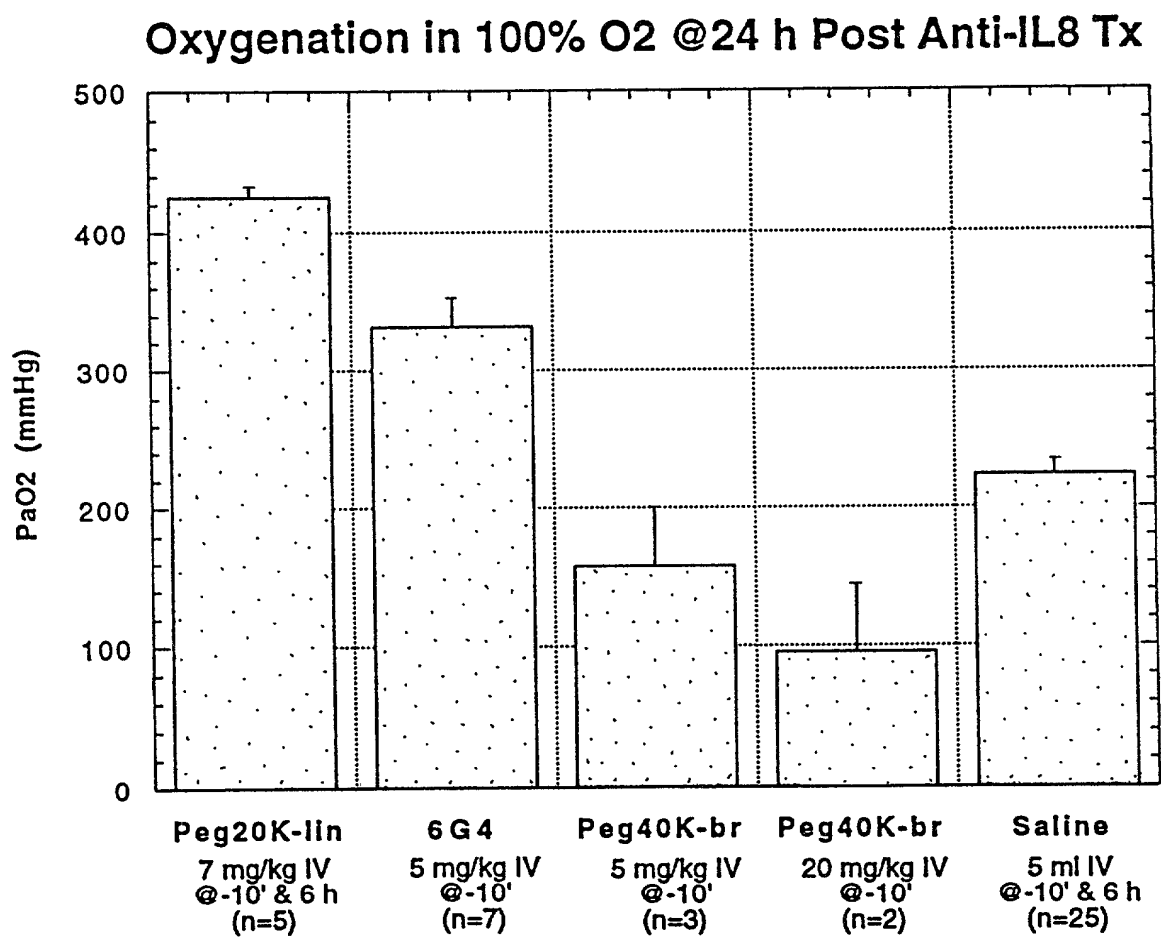


FIG. 70A

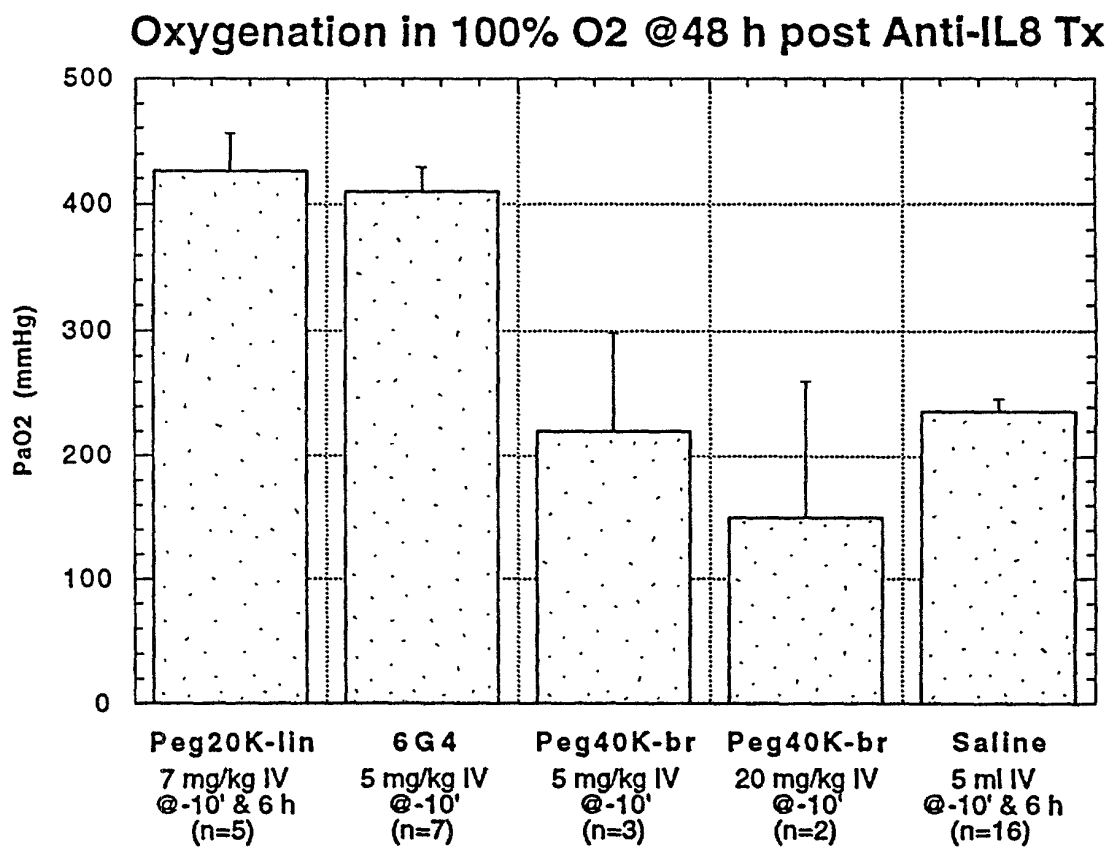


FIG. 70B

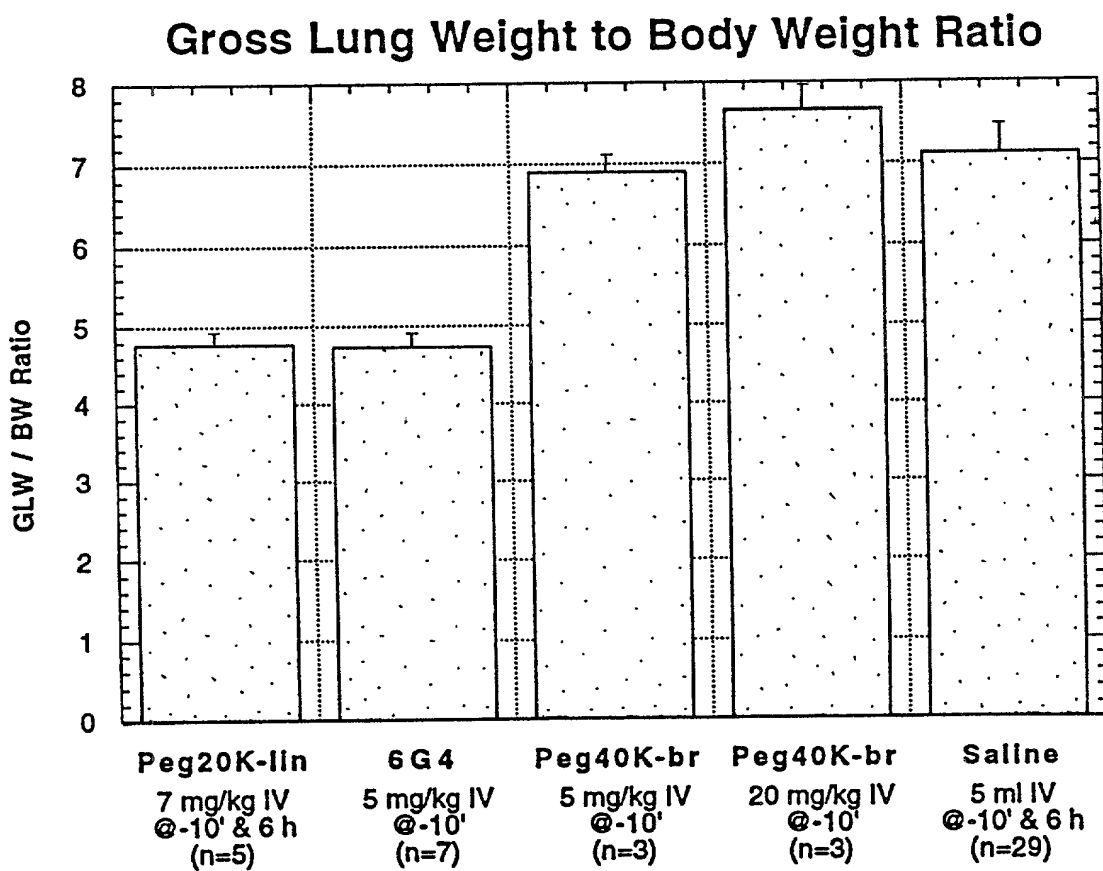


FIG. 70C

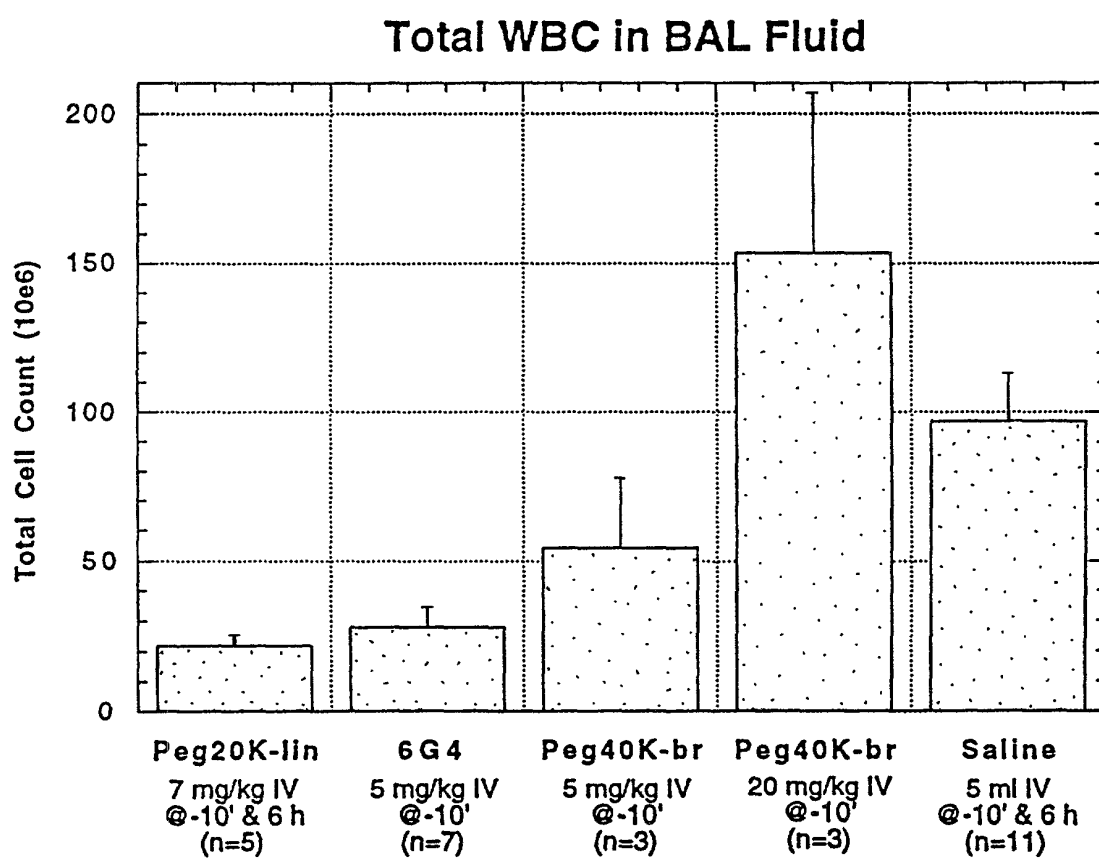


FIG. 70D

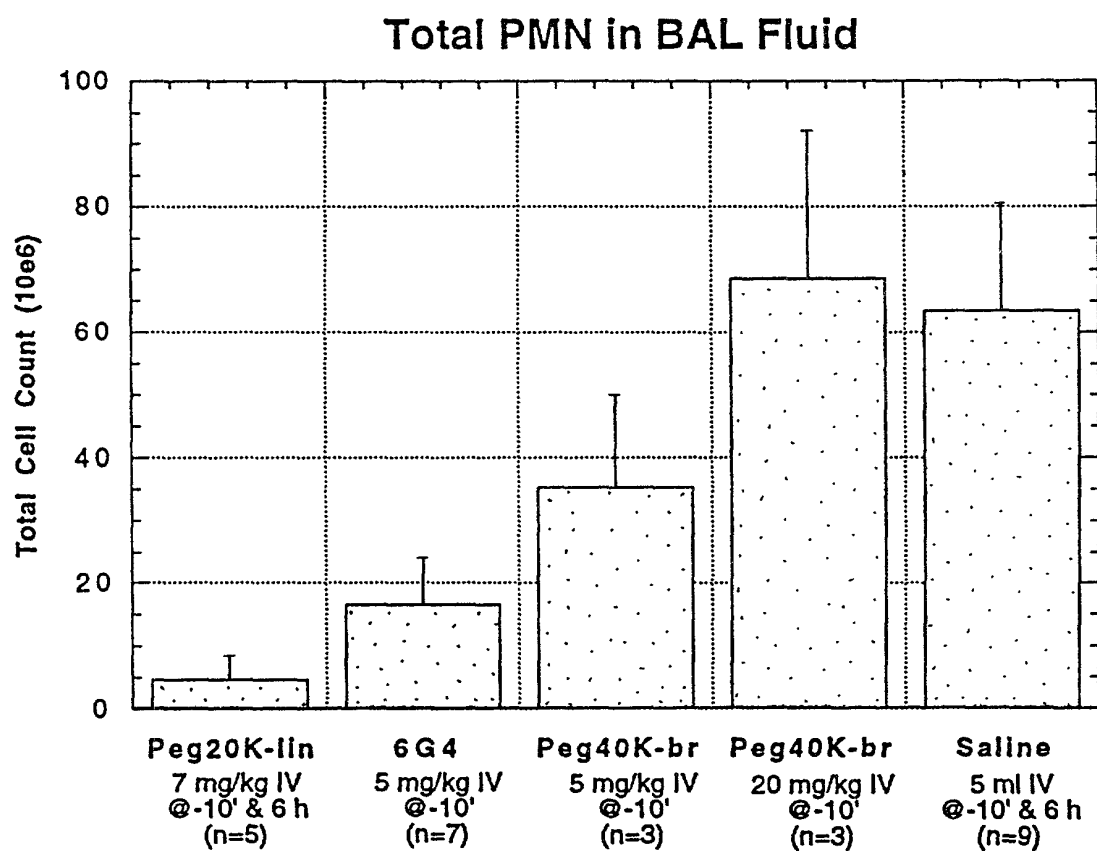
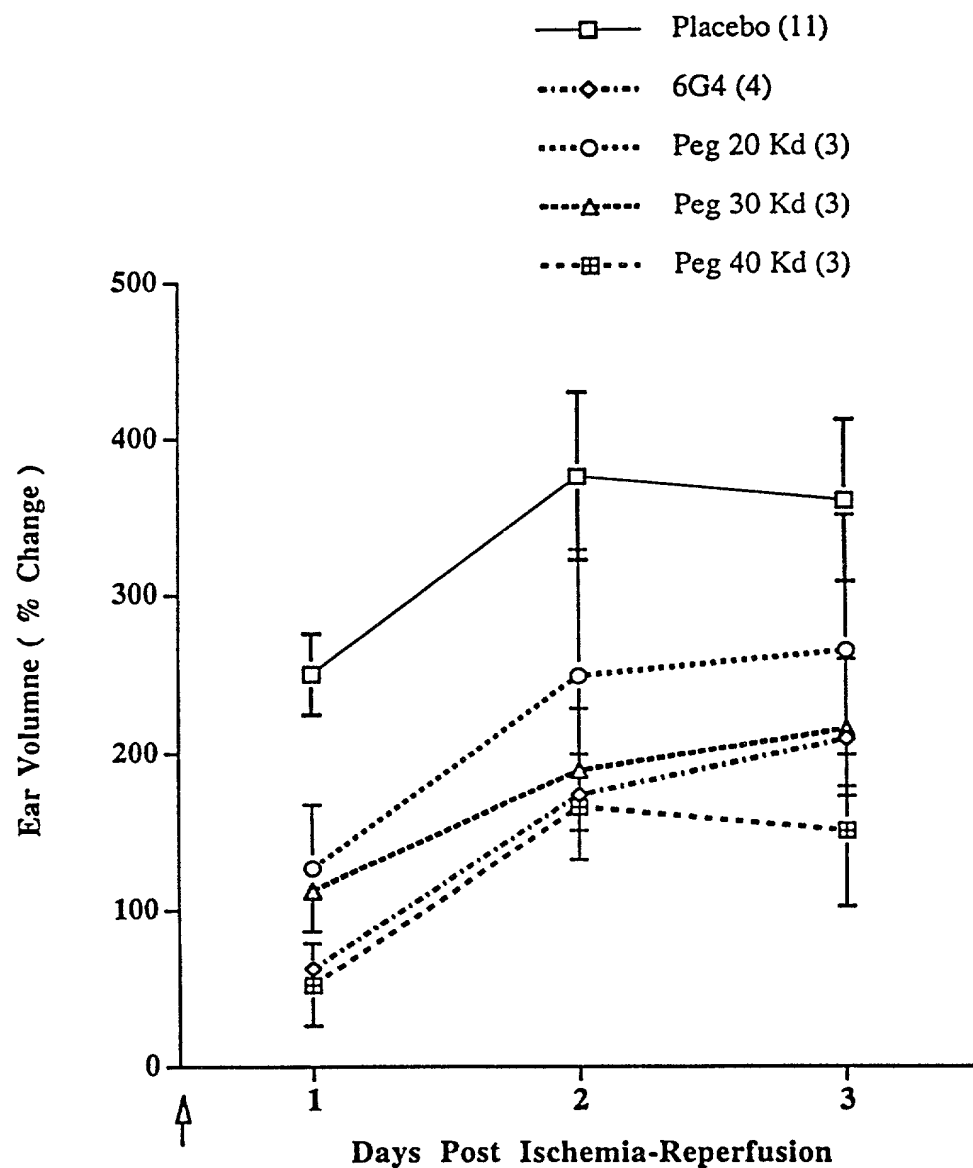


FIG. 70E

The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations :
Single Dose (5 mg/kg)
administered IV at time
of reperfusion

FIG. 71